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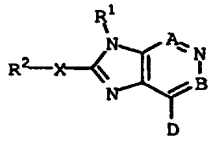

(I)

(57) Abstract

The present invention describes novel imidazo–pyridines, –pyridazines, and –triazines of formula (I) wherein A and B can be C or N and D is aryl or heteroaryl or pharmaceutically acceptable salt forms thereof, which are useful as CRF antagonists.

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TITLE

IMIDAZO-PYRIDINES, -PYRIDAZINES, AND -TRIAZINES AS CORTICOTROPIN RELEASING FACTOR ANTAGONISTS

FIELD OF THE INVENTION

This invention relates to novel imidazo-pyridines, -pyridazines, and -triazines, pharmaceutical compositions containing the same and methods of using same in the treatment of psychiatric disorders and neurological diseases including affective disorder, anxiety, depression, headache, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, epilepsy, stroke, ulcers, amyotrophic lateral sclerosis, hypoglycemia or a disorder the treatment of which can be effected or facilitated by antagonizing corticotropin releasing factor (CRF), including but not limited to disorders induced or facilitated by CRF.

BACKGROUND OF THE INVENTION

Corticotropin releasing factor, a 41 amino acid peptide, is the primary physiological regulator of proopiomelanocortin (POMC)-derived peptide secretion from the anterior pituitary gland [J. Rivier et al., *Proc. Nat. Acad. Sci. (USA)* 80:4851 (**1983**); W. Vale et al., *Science* 213:1394 (**1981**)]. In addition to its endocrine role at the pituitary gland, immunohistochemical localization of CRF has demonstrated that the hormone has a broad extrahypothalamic distribution in the central nervous system and produces a wide spectrum of autonomic, electrophysiological and behavioral effects consistent with a neurotransmitter or neuromodulator role in brain [W. Vale et al., *Rec. Prog. Horm. Res.* 39:245 (**1983**); G.F. Koob, *Persp. Behav. Med.* 2:39 (**1985**); E.B. De Souza et

al., *J. Neurosci.* 5:3189 (**1985**)]. There is also evidence that CRF plays a significant role in integrating the response of the immune system to physiological, psychological, and immunological stressors [J.E. Blalock, *Physiological Reviews* 69:1 (**1989**); J.E. Morley, *Life Sci.* 41:527 (**1987**)].

Clinical data provides evidence that CRF has a role in psychiatric disorders and neurological diseases including depression, anxiety-related disorders and feeding disorders. A role for CRF has also been postulated in the etiology and pathophysiology of Alzheimer's disease, Parkinson's disease, Huntington's disease, progressive supranuclear palsy and amyotrophic lateral sclerosis as they relate to the dysfunction of CRF neurons in the central nervous system [for review see E.B. De Souza, *Hosp. Practice* 23:59 (**1988**)].

In affective disorder, or major depression, the concentration of CRF is significantly increased in the cerebral spinal fluid (CSF) of drug-free individuals [C.B. Nemeroff et al., *Science* 226:1342 (**1984**); C.M. Banki et al., *Am. J. Psychiatry* 144:873 (**1987**); R.D. France et al., *Biol. Psychiatry* 28:86 (**1988**); M. Arato et al., *Biol Psychiatry* 25:355 (**1989**)]. Furthermore, the density of CRF receptors is significantly decreased in the frontal cortex of suicide victims, consistent with a hypersecretion of CRF [C.B. Nemeroff et al., *Arch. Gen. Psychiatry* 45:577 (**1988**)]. In addition, there is a blunted adrenocorticotropin (ACTH) response to CRF (i.v. administered) observed in depressed patients [P.W. Gold et al., *Am J. Psychiatry* 141:619 (**1984**); F. Holsboer et al., *Psychoneuroendocrinology* 9:147 (**1984**); P.W. Gold et al., *New Eng. J. Med.* 314:1129 (**1986**)]. Preclinical studies in rats and non-human primates provide additional support for the hypothesis that hypersecretion of CRF may be involved in the symptoms seen in human depression [R.M. Sapolsky, *Arch. Gen. Psychiatry* 46:1047 (**1989**)]. There is preliminary evidence that tricyclic antidepressants can alter CRF levels and thus modulate the numbers of CRF receptors in brain [Grigoriadis et al., *Neuropsychopharmacology* 2:53 (**1989**)].

There has also been a role postulated for CRF in the etiology of anxiety-related disorders. CRF produces anxiogenic effects in animals and interactions between benzodiazepine/non-benzodiazepine anxiolytics and CRF have been demonstrated in a variety of behavioral anxiety models [D.R. Britton et al., *Life Sci.* 31:363 (**1982**); C.W. Berridge and A.J. Dunn *Regul. Peptides* 16:83 (**1986**)]. Preliminary studies using the putative CRF receptor antagonist α-helical ovine CRF (9-41) in a variety of behavioral paradigms demonstrate that the antagonist produces "anxiolytic-like" effects that are qualitatively similar to the benzodiazepines [C.W. Berridge and A.J. Dunn, *Horm. Behav.* 21:393 (**1987**), *Brain Research Reviews* 15:71 (**1990**)]. Neurochemical, endocrine and receptor binding studies have all demonstrated interactions between CRF and benzodiazepine anxiolytics providing further evidence for the involvement of CRF in these disorders. Chlordiazepoxide attenuates the "anxiogenic" effects of CRF in both the conflict test [K.T. Britton et al., *Psychopharmacology* 86:170 (**1985**); K.T. Britton et al., *Psychopharmacology* 94:306 (**1988**)] and in the acoustic startle test [N.R. Swerdlow et al., *Psychopharmacology* 88:147 (**1986**)] in rats. The benzodiazepine receptor antagonist (Ro15-1788), which was without behavioral activity alone in the operant conflict test, reversed the effects of CRF in a dose-dependent manner while the benzodiazepine inverse agonist (FG7142) enhanced the actions of CRF [K.T. Britton et al., *Psychopharmacology* 94:306 (**1988**)].

The mechanisms and sites of action through which the standard anxiolytics and antidepressants produce their therapeutic effects remain to be elucidated. It has been hypothesized however, that they are involved in the suppression of the CRF hypersecretion that is observed in these disorders. Of particular interest is that preliminary studies examining the effects of a CRF receptor antagonist (α-helical CRF_{9-41}) in a variety of behavioral paradigms have demonstrated that the CRF antagonist produces "anxiolytic-like" effects qualitatively similar to the benzodiazepines [for review see G.F. Koob and K.T. Britton,

In: *Corticotropin-Releasing Factor: Basic and Clinical Studies of a Neuropeptide*, E.B. De Souza and C.B. Nemeroff eds., CRC Press p221 (1990)].

In view of the above, efficacious and specific antagonists of CRF are desired as potentially valuable therapeutic agents for the treatment of psychiatric disorders and neurological diseases. It is thus desirable to discover new CRF antagonists.

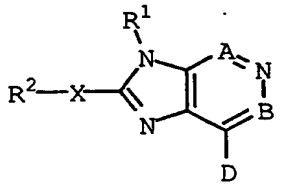
SUMMARY OF THE INVENTION

Accordingly, one object of the present invention is to provide novel imidazo-pyridines, -pyridazines, and -triazines, which are useful as CRF antagonists or pharmaceutically acceptable salts or prodrugs thereof.

It is another object of the present invention to provide pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt form thereof.

It is another object of the present invention to provide a method for treating psychiatric disorders and neurological diseases comprising administering to a host in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt form thereof.

These and other objects, which will become apparent during the following detailed description, have been achieved by the inventors' discovery that compounds of formula I:

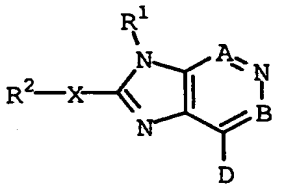


(I)

or pharmaceutically acceptable salt forms thereof, wherein R^1, R^2, R^3, and R^4 are defined below, are CRF antagonists.

DETAILED DESCRIPTION OF THE INVENTION

[1] Thus, in a first embodiment, the present invention provides a novel compound of formula I:



(I)

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

A is N or C-R^7;

B is N or C-R^8;

D is an aryl or heteroaryl group attached through an unsaturated carbon atom;

X is selected from the group CH-R^9, N-R^{10}, O, $S(O)_n$ and a bond;

n is 0, 1 or 2;

R^1 is selected from the group C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-8} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-4} alkoxy-C_{1-4} alkyl, $-SO_2-C_{1-10}$ alkyl, $-SO_2-R^{1a}$, and $-SO_2-R^{1b}$;

R^1 is substituted with 0-1 substituents selected from the group -CN, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-CO_2R^{13a}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-CONR^{13a}R^{16a}$, 1-morpholinyl, 1-piperidinyl, 1-piperazinyl, and C_{3-8} cycloalkyl, wherein 0-1 carbon atoms in the C_{4-8} cycloalkyl is replaced by a group selected from the group -O-, $-S(O)_n-$, $-NR^{13a}-$, $-NCO_2R^{14b}-$, $-NCOR^{14b}-$ and $-NSO_2R^{14b}-$, and wherein N_4 in 1-piperazinyl is

substituted with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^1 is also substituted with 0-3 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, R^{1c}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, I, C_{1-4} haloalkyl, $-OR^{13a}$, $-NR^{13a}R^{16a}$, C_{1-4} alkoxy-C_{1-4} alkyl, and C_{3-8} cycloalkyl which is substituted with 0-1 R^9 and in which 0-1 carbons of C_{4-8} cycloalkyl is replaced by -O-;

provided that R^1 is other than a cyclohexyl-$(CH_2)_2$- group;

R^{1a} is aryl and is selected from the group phenyl, naphthyl, indanyl and indenyl, each R^{1a} being substituted with 0-1 $-OR^{17}$ and 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$;

R^{1b} is heteroaryl and is selected from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-onyl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$ and each heteroaryl being substituted on any nitrogen

atom with 0-1 substituents selected from the group R^{15a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^{1c} is heterocyclyl and is a saturated or partially saturated heteroaryl, each heterocyclyl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{13a}$, SH, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-OC(O)R^{14b}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-NR^{13a}R^{16a}$, and $-CONR^{13a}R^{16a}$ and each heterocyclyl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b} and wherein any sulfur atom is optionally monooxidized or dioxidized;

provided that R^1 is other than a $-(CH_2)_{1-4}$-aryl, $-(CH_2)_{1-4}$-heteroaryl, or $-(CH_2)_{1-4}$-heterocycle, wherein the aryl, heteroaryl, or heterocycle group is substituted or unsubstituted;

R^2 is selected from the group C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{2-4} alkenyl, and C_{2-4} alkynyl and is substituted with 0-3 substituents selected from the group -CN, hydroxy, halo and C_{1-4} alkoxy;

alternatively R^2, in the case where X is a bond, is selected from the group -CN, CF_3 and C_2F_5;

R^7 and R^8 are independently selected at each occurrence from the group H, Br, Cl, F, I, -CN, C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, $(C_{1-4}$ alkyl$)_2$amino and phenyl, each phenyl is substituted with 0-3 groups selected from the group C_{1-7} alkyl, C_{3-8} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkyl

sulfinyl, C_{1-4} alkylsulfonyl, C_{1-6} alkylamino and (C_{1-4} alkyl)$_2$amino;

R^9 and R^{10} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-6} cycloalkyl-C_{1-4} alkyl and C_{3-8} cycloalkyl;

R^{13} is selected from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, aryl, aryl(C_{1-4} alkyl)-, heteroaryl and heteroaryl(C_{1-4} alkyl)-;

R^{13a} and R^{16a} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{14} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, aryl, aryl(C_{1-4} alkyl)-, heteroaryl and heteroaryl(C_{1-4} alkyl)- and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy C_{1-4} haloalkoxy, and dimethylamino;

R^{14a} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{14b} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{15} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, phenyl and benzyl, each phenyl or benzyl being substituted on the aryl moiety with 0-3 groups chosen from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{15a} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{17} is selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{1-4} haloalkyl, $R^{14}S(O)_n$-C_{1-4} alkyl, and $R^{17b}R^{19b}N$-C_{2-4} alkyl;

R^{18} and R^{19} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{1-4} haloalkyl;

alternatively, in an $NR^{17}R^{19}$ moiety, R^{17} and R^{19} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

alternatively, in an $NR^{17b}R^{19b}$ moiety, R^{17b} and R^{19b} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

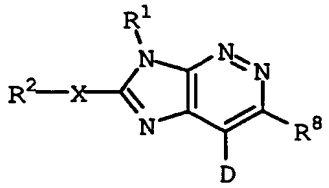
R^{17a} and R^{19a} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and C_{1-4} haloalkyl;

aryl is independently selected at each occurrence from the group phenyl, naphthyl, indanyl and indenyl, each aryl being substituted with 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, methylenedioxy, C_{1-4} alkoxy-C_{1-4} alkoxy, $-OR^{17}$, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, $-NO_2$, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and up to 1 phenyl, each phenyl substituent being substituted with 0-4 substituents selected from the group C_{1-3} alkyl, C_{1-3} alkoxy, Br, Cl, F, I, -CN, dimethylamino, CF_3, C_2F_5, OCF_3, SO_2Me and acetyl;

heteroaryl is independently selected at each occurence from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-on-yl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15}, CO_2R^{14a}, COR^{14a} and SO_2R^{14a}; and,

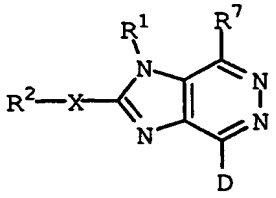
provided that when D is imidazole or triazole, R^1 is other than unsubstituted C_{1-6} linear or branched alkyl or C_{3-6} cycloalkyl.

[2] In a preferred embodiment, the present invention provides a novel compound of formula Ia:



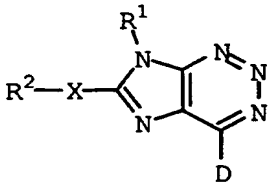
(Ia).

[3] In another preferred embodiment, the present invention provides a novel compound of formula Ib:



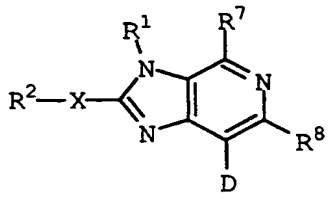
(Ib).

[4] In another preferred embodiment, the present invention provides a novel compound of formula Ic:



(Ic).

[5] In another preferred embodiment, the present invention provides a novel compound of formula Id:



(Id).

[5a] In a more preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

X is selected from the group O, $S(O)_n$ and a bond;

n is 0, 1 or 2;

R^1 is selected from the group C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{3-8} cycloalkyl;

R^1 is substituted with 0-1 substituents selected from the group -CN, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-CO_2R^{13a}$, and C_{3-8} cycloalkyl, wherein 0-1 carbon atoms in the C_{4-8} cycloalkyl is replaced by a group selected from the group -O-, $-S(O)_n-$, $-NR^{13a}-$, $-NCO_2R^{14b}-$, $-NCOR^{14b}-$ and $-NSO_2R^{14b}-$;

R^1 is also substituted with 0-2 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, CF_3, CF_2CF_3, $-OR^{13a}$, $-NR^{13a}R^{16a}$, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{3-8} cycloalkyl which is substituted with 0-1 R^9 and in which 0-1 carbons of C_{4-8} cycloalkyl is replaced by -O-;

provided that R^1 is other than a cyclohexyl-$(CH_2)_2$- group;

R^{1a} is aryl and is selected from the group phenyl and indanyl, each R^{1a} being substituted with 0-1 $-OR^{17}$ and 0-5 substituents independently selected at each occurrence from the group C_{1-4} alkyl, C_{3-6} cycloalkyl, Br, Cl, F,

C_{1-4} haloalkyl, -CN, $-S(O)_nR^{18}$, $-COR^{17}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$;

R^{1b} is heteroaryl and is selected from the group pyridyl, pyrimidinyl, furanyl, thienyl, imidazolyl, thiazolyl, pyrrolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, and indazolyl, each heteroaryl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-4} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, CF_3, -CN, $-OR^{17}$, $-S(O)_mR^{18}$, $-COR^{17}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

provided that R^1 is other than a $-(CH_2)_{1-4}$-aryl or $-(CH_2)_{1-4}$-heteroaryl wherein the aryl or heteroaryl group is substituted or unsubstituted;

R^2 is selected from the group C_{1-4} alkyl, C_{2-4} alkenyl, and C_{2-4} alkynyl and is substituted with 0-1 substituents selected from the group -CN, OH, Cl, F, and C_{1-4} alkoxy;

R^7 and R^8 are independently selected from the group H, Br, Cl, F, -CN, C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{1-4} alkoxy, NH_2, C_{1-4} alkylamino, and $(C_{1-4}$ alkyl$)_2$-amino;

R^9 is independently selected at each occurrence from the group H, C_{1-4} alkyl and C_{3-8} cycloalkyl;

R^{13} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{3-6} cycloalkyl-C_{1-2} alkyl, aryl(C_{1-2} alkyl)-, and heteroaryl(C_{1-2} alkyl)-;

R^{13a} and R^{16a} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{14} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{3-6} cycloalkyl-C_{1-2} alkyl, aryl(C_{1-2} alkyl)-, and heteroaryl(C_{1-2} alkyl)-;

R^{14a} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{3-6} cycloalkyl-C_{1-2} alkyl;

R^{14b} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-2} alkyl;

R^{15} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, phenyl and benzyl, each phenyl or benzyl being substituted on the aryl moiety with 0-3 groups chosen from the group C_{1-4} alkyl, Br, Cl, F, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{15a} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{17}, R^{18} and R^{19} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{1-4} haloalkyl;

alternatively, in an $NR^{17}R^{19}$ moiety, R^{17} and R^{19} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

R^{17a} and R^{19a} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and C_{1-4} haloalkyl;

aryl is phenyl substituted with 1-4 substituents independently selected at each occurrence from the group C_{1-4} alkyl, C_{3-6} cycloalkyl, $-OR^{17}$, Br, Cl, F, C_{1-4} haloalkyl, -CN, $-S(O)_nR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-NR^{15}COR^{17}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$; and,

heteroaryl is independently selected at each occurence from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-on-yl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted 1-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, C_{1-4} haloalkyl, -CN, $-OR^{17}$, $-S(O)_mR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15}, CO_2R^{14a}, COR^{14a} and SO_2R^{14a}.

[5b] In an even more preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

X is selected from the group O, S and a bond

R^1 is substituted C_{1-6} alkyl;

R^1 is substituted with 0-1 substituents selected from the group -CN, $-CO_2R^{13a}$, and C_{3-8} cycloalkyl, wherein 0-1 carbon atoms in the C_{4-8} cycloalkyl is replaced by a group selected from the group -O-, $-S(O)_n-$, and $-NR^{13a}-$;

R^1 is also substituted with 0-2 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, CF_3, $-OR^{13a}$, $-NR^{13a}R^{16a}$, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{3-6} cycloalkyl which is substituted with 0-1 CH_3 and in which 0-1 carbons of C_{4-8} cycloalkyl is replaced by -O-;

provided that R^1 is other than a cyclohexyl-$(CH_2)_2$- group;

R^{1a} is aryl and is phenyl substituted with 0-1 substituents selected from OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, and OCF_3, and 0-3 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, Br, Cl, F, CF_3, -CN, SCH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$;

R^{1b} is heteroaryl and is selected from the group furanyl, thienyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, and indazolyl, each heteroaryl being substituted on 0-3 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group CH_3, CO_2CH_3, $COCH_3$ and SO_2CH_3;

provided that R^1 is other than a $-(CH_2)_{1-4}$-aryl or $-(CH_2)_{1-4}$-heteroaryl wherein the aryl or heteroaryl group is substituted or unsubstituted;

R^2 is selected from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, and $CH_2CH_2CH_3$;

R^7 and R^8 are independently selected from the group H, CH_3, CH_2CH_3, $CH(CH_3)_2$, and $CH_2CH_2CH_3$;

aryl is phenyl substituted with 2-4 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$; and,

heteroaryl is independently selected at each occurence from the group pyridyl, indolyl, benzothienyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, and benzoxazolin-2-on-yl, each heteroaryl being substituted on 2-4 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group CH_3, CO_2CH_3, $COCH_3$ and SO_2CH_3.

[5c] In a still more preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

R^1 is substituted C_1;

R^1 is substituted with 0-1 substituents selected from the group -CN, $-CO_2CH_3$, and $-CO_2CH_2CH_3$;

R^1 is also substituted with 0-2 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, $-(CH_2)_3CH_3$, $-CH=CH_2$, $-CH=CH(CH_3)$, $-CH\equiv CH$, $-CH\equiv C(CH_3)$, CH_2OCH_3, $-CH_2CH_2OCH_3$, F, CF_3, cyclopropyl, CH_3-cyclopropyl, cyclobutyl, CH_3-cyclobutyl, cyclopentyl, CH_3-cyclopentyl;

R^{1a} is phenyl substituted with 0-1 substituents selected from OCH_3, OCH_2CH_3, and OCF_3, and 0-2 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, Br, Cl, F, CF_3, -CN, and SCH_3;

R^{1b} is heteroaryl and is selected from the group furanyl, thienyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, and tetrazolyl, each heteroaryl being substituted on 0-3 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, OCH_3, OCH_2CH_3, OCF_3, Br, Cl, F, CF_3, -CN, and SCH_3 and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group CH_3, CO_2CH_3, $COCH_3$ and SO_2CH_3;

provided that R^1 is other than a $-(CH_2)_{1-4}$-aryl or $-(CH_2)_{1-4}$-heteroaryl wherein the aryl or heteroaryl group is substituted or unsubstituted;

R^2 is selected from the group CH_3, CH_2CH_3, and $CH(CH_3)_2$;

R^7 and R^8 are independently selected from the group H and CH_3;

aryl is phenyl substituted with 2-4 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$; and,

heteroaryl is pyridyl substituted on 2-4 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$.

[5d] In a further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

R^1 is substituted (cyclopropyl)-C_1 alkyl or (cyclobutyl)-C_1 alkyl;

R^1 is substituted with 0-1 -CN;

R^1 is also substituted with 0-1 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, $-(CH_2)_3CH_3$, $-CH=CH_2$, $-CH=CH(CH_3)$, $-CH\equiv CH$, $-CH\equiv C(CH_3)$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, F, CF_3, cyclopropyl, and CH_3-cyclopropyl;

R^{1a} is phenyl substituted with 0-1 substituents selected from OCH_3, OCH_2CH_3, and OCF_3, and 0-2 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, Br, Cl, F, CF_3, -CN, and SCH_3;

R^{1b} is heteroaryl and is selected from the group furanyl, thienyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, and pyrazolyl, each heteroaryl being substituted on 0-3 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, OCH_3, OCH_2CH_3, OCF_3, Br, Cl, F, CF_3, -CN, and SCH_3.

[5e] In another further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

R^1 is (cyclopropyl)C_1 alkyl or (cyclobutyl)-C_1 alkyl substituted with 1 substituent independently selected at each occurrence from the group R^{1a}, R^{1b}, CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, $-(CH_2)_3CH_3$, $-CH=CH_2$, $-CH=CH(CH_3)$, -

$CH{\equiv}CH$, $-CH{\equiv}C(CH_3)$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, F, CF_3, cyclopropyl, and CH_3-cyclopropyl;

R^{1a} is phenyl substituted with 0-2 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, Cl, F, and CF_3;

R^{1b} is heteroaryl and is selected from the group furanyl, thienyl, and isoxazolyl, each heteroaryl being substituted on 0-2 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, OCH_3, Cl, F, and CF_3.

[5f] In an even further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

R^1 is selected from the group

R^1 is selected from the group (cyclopropyl)CH-CH_3, (cyclopropyl)CH-CH_2CH_3, (cyclopropyl)CH-CH_2OCH_3, (cyclopropyl)CH-$CH_2CH_2CH_3$, (cyclopropyl)CH-$CH_2CH_2OCH_3$, (cyclopropyl)$_2$CH, phenyl(cyclopropyl)CH, furanyl(cyclopropyl)CH, thienyl(cyclopropyl)CH, isoxazolyl(cyclopropyl)CH, (CH_3-furanyl)(cyclopropyl)CH, (cyclobutyl)CH-CH_3, (cyclobutyl)CH-CH_2CH_3, (cyclobutyl)CH-CH_2OCH_3, (cyclobutyl)CH-$CH_2CH_2CH_3$, (cyclobutyl)CH-$CH_2CH_2OCH_3$, (cyclobutyl)$_2$CH, phenyl(cyclobutyl)CH, furanyl(cyclobutyl)CH, thienyl(cyclobutyl)CH, isoxazolyl(cyclobutyl)CH, and (CH_3-furanyl)(cyclobutyl)CH;

[5g] In another further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

D is phenyl substituted with 2-4 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3,

$CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, and CF_3.

[5h] In another further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

D is pyridyl substituted on 2-4 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, and CF_3.

[5i] In another preferred embodiment, the present invention provides a novel compound of formula Id, wherein the compound is selected from the group:

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-ethyl)propyl-imidazo[4,5-c]pyridine;

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-c]pyridine;

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-c]pyridine;

4-(2,4-Dichlorophenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-c]pyridine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-c]pyridine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-c]pyridine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-c]pyridine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-c]pyridine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-c]pyridine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-c]pyridine;

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-c]pyridine;

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-c]pyridine;

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-c]pyridine;

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-ethyl)propyl-imidazo[4,5-d]pyridazine;

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-d]pyridazine;

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-d]pyridazine;

4-(2,4-Dichlorophenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-d]pyridazine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-d]pyridazine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-d]pyridazine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-d]pyridazine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-d]pyridazine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-d]pyridazine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-d]pyridazine;

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-d]pyridazine;

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-d]pyridazine;

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-d]pyridazine;

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-ethyl)propyl-imidazo[4,5-c]pyridazine;

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-c]pyridazine;

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-c]pyridazine;

4-(2,4-Dichlorophenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-c]pyridazine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-c]pyridazine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-c]pyridazine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-c]pyridazine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-c]pyridazine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-c]pyridazine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-c]pyridazine;

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-c]pyridazine;

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-c]pyridazine;

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-c]pyridazine;

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-ethyl)propyl-imidazo[4,5-d]triazine;

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-d]triazine;

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-d]triazine;

4-(2,4-Dichlorophenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-d]triazine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-d]triazine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-d]triazine;

4-(2-Chloro-4-trifluoromethylphenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-d]triazine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-d]triazine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-d]triazine;

4-(2-Chloro-4-methoxyphenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-d]triazine;

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-d]triazine;

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-1-(1-cyclopropyl)butyl-imidazo[4,5-d]triazine; and,

4-(2-Methyl-4-methoxy-5-fluorophenyl)-2-ethyl-3-(1-methoxy)butyl-imidazo[4,5-d]triazine;

or a pharmaceutically acceptable salt form thereof.

[5j] In another more preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

R^1 is C_{3-8} cycloalkyl;

R^1 is substituted with 0-1 substituents selected from the group -CN, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-CO_2R^{13a}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-CONR^{13a}R^{16a}$, 1-morpholinyl, 1-piperidinyl, 1-piperazinyl, and C_{4-8} cycloalkyl, wherein 0-1 carbon atoms in the C_{4-8} cycloalkyl is replaced by a group selected from the group

-O-, -S(O)$_n$-, -NR^{13a}-, -NCO$_2$R^{14b}-, -NCOR^{14b}- and -NSO$_2$R^{14b}-, and wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13a}, CO$_2$R^{14b}, COR^{14b} and SO$_2$R^{14b}; and,

R^1 is also substituted with 0-3 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, R^{1c}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, I, C_{1-4} haloalkyl, -OR^{13a}, C_{1-2} alkoxy-C_{1-2} alkyl, and -NR^{13a}R^{16a}.

[5k] In another even more preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

X is selected from the group O, S(O)$_n$ and a bond;

n is 0, 1 or 2;

R^1 is selected from the group cyclopropyl, cyclobutyl, and cyclopentyl;

R^1 is substituted with 0-1 substituents selected from the group -CN, -S(O)$_n$R^{14b}, -COR^{13a}, -CO$_2$R^{13a}, and C_{4-8} cycloalkyl, wherein one carbon atom in the C_{4-8} cycloalkyl is replaced by a group selected from the group -O-, -S(O)$_n$-, -NR^{13a}-, -NCO$_2$R^{14b}-, -NCOR^{14b}- and -NSO$_2$R^{14b}-;

R^1 is also substituted with 0-2 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, CF_3, CF_2CF_3, -OR^{13a}, C_{1-2} alkoxy-C_{1-2} alkyl, and -NR^{13a}R^{16a};

R^{1a} is aryl and is selected from the group phenyl and indanyl, each R^{1a} being substituted with 0-1 -OR^{17} and 0-5 substituents independently selected at each occurrence from the group C_{1-4} alkyl, C_{3-6} cycloalkyl, Br, Cl, F,

C_{1-4} haloalkyl, -CN, $-S(O)_nR^{18}$, $-COR^{17}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$;

R^{1b} is heteroaryl and is selected from the group pyridyl, pyrimidinyl, furanyl, thienyl, imidazolyl, thiazolyl, pyrrolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, and indazolyl, each heteroaryl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-4} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, CF_3, -CN, $-OR^{17}$, $-S(O)_mR^{18}$, $-COR^{17}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^2 is selected from the group C_{1-4} alkyl, C_{2-4} alkenyl, and C_{2-4} alkynyl and is substituted with 0-1 substituents selected from the group -CN, OH, Cl, F, and C_{1-4} alkoxy;

R^9 is independently selected at each occurrence from the group H, C_{1-4} alkyl and C_{3-8} cycloalkyl;

R^7 and R^8 are independently selected from the group H, Br, Cl, F, -CN, C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{1-4} alkoxy, NH_2, C_{1-4} alkylamino, and $(C_{1-4}$ alkyl$)_2$-amino;

R^{13} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{3-6} cycloalkyl-C_{1-2} alkyl, aryl(C_{1-2} alkyl)-, and heteroaryl(C_{1-2} alkyl)-;

R^{13a} and R^{16a} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{14} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{3-6} cycloalkyl-C_{1-2} alkyl, aryl(C_{1-2} alkyl)-, and heteroaryl(C_{1-2} alkyl)-;

R^{14a} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{3-6} cycloalkyl-C_{1-2} alkyl;

R^{14b} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-2} alkyl;

R^{15} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, phenyl and benzyl, each phenyl or benzyl being substituted on the aryl moiety with 0-3 groups chosen from the group C_{1-4} alkyl, Br, Cl, F, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{15a} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{17}, R^{18} and R^{19} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{1-4} haloalkyl;

alternatively, in an $NR^{17}R^{19}$ moiety, R^{17} and R^{19} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

R^{17a} and R^{19a} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and C_{1-4} haloalkyl;

aryl is phenyl substituted with 1-4 substituents independently selected at each occurrence from the group C_{1-4} alkyl, C_{3-6} cycloalkyl, $-OR^{17}$, Br, Cl, F, C_{1-4} haloalkyl, -CN,

$-S(O)_nR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-NR^{15}COR^{17}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$; and,

heteroaryl is independently selected at each occurence from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-on-yl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted 1-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, C_{1-4} haloalkyl, -CN, $-OR^{17}$, $-S(O)_mR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15}, CO_2R^{14a}, COR^{14a} and SO_2R^{14a}.

[51] In another still more preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

X is selected from the group O, S and a bond

R^1 is substituted with 0-1 substituents selected from the group -CN, $-CO_2R^{13a}$, and C_{4-8} cycloalkyl, wherein 0-1 carbon atoms in the C_{4-8} cycloalkyl is replaced by a group selected from the group -O-, $-S(O)_n-$, and $-NR^{13a}-$;

R^1 is also substituted with 0-2 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, CF_3, CF_3, $-OR^{13a}$, -OH, $-OCH_3$, $-OCH_2CH_3$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, and $-NR^{13a}R^{16a}$;

R^{1a} is aryl and is phenyl substituted with 0-1 substituents selected from OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, and OCF_3, and 0-3 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, Br, Cl, F, CF_3, -CN, SCH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$;

R^{1b} is heteroaryl and is selected from the group furanyl, thienyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, and indazolyl, each heteroaryl being substituted on 0-3 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group CH_3, CO_2CH_3, $COCH_3$ and SO_2CH_3;

R^2 is selected from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, and $CH_2CH_2CH_3$;

R^7 and R^8 are independently selected from the group H, CH_3, CH_2CH_3, $CH(CH_3)_2$, and $CH_2CH_2CH_3$;

aryl is phenyl substituted with 2-4 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$; and,

heteroaryl is independently selected at each occurence from the group pyridyl, indolyl, benzothienyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, and

benzoxazolin-2-on-yl, each heteroaryl being substituted on 2-4 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group CH_3, CO_2CH_3, $COCH_3$ and SO_2CH_3.

[5m] In another further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

R^1 is substituted with 0-2 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, $-(CH_2)_3CH_3$, $-CH=CH_2$, $-CH=CH(CH_3)$, $-CH\equiv CH$, $-CH\equiv C(CH_3)$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, F, and CF_3;

R^{1a} is phenyl substituted with 0-1 substituents selected from OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, and OCF_3, and 0-2 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, Br, Cl, F, CF_3, -CN, and SCH_3;

R^{1b} is heteroaryl and is selected from the group furanyl, thienyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, and tetrazolyl, each heteroaryl being substituted on 0-3 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, OCH_3, OCH_2CH_3, OCF_3, Br, Cl, F, CF_3, -CN, and SCH_3 and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group CH_3, CO_2CH_3, $COCH_3$ and SO_2CH_3;

R^2 is selected from the group CH_3, CH_2CH_3, and $CH(CH_3)_2$;

R^7 and R^8 are independently selected from the group H and CH_3;

aryl is phenyl substituted with 2-4 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$; and,

heteroaryl is pyridyl substituted on 2-4 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$.

[5n] In another even further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

R^1 is substituted with 0-2 substituents independently selected at each occurrence from the group R^{1a}, CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, $-(CH_2)_3CH_3$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, F, and CF_3; and,

R^{1a} is phenyl substituted with 0-2 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, Br, Cl, F, CF_3, -CN, and SCH_3.

[5o] In a still further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

D is phenyl substituted with 2-4 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, and CF_3.

[5p] In another still further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

D is pyridyl substituted on 2-4 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, and CF_3.

[5q] In another more preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

R^1 is selected from the group C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-8} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and C_{1-4} alkoxy-C_{1-4} alkyl;

R^1 is substituted with a C_{3-8} cycloalkyl group, wherein 0-1 carbon atoms in the C_{4-8} cycloalkyl group is replaced by a group selected from the group -O-, $-S(O)_n-$, $-NR^{13a}-$, $-NCO_2R^{14b}-$, $-NCOR^{14b}-$ and $-NSO_2R^{14b}-$;

R^1 is also substituted with 0-3 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, R^{1c}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, I, C_{1-4} haloalkyl, $-OR^{13a}$, $-NR^{13a}R^{16a}$, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{3-8} cycloalkyl which is substituted with 0-1 R^9 and in which 0-1 carbons of C_{4-8} cycloalkyl is replaced by -O-;

provided that R^1 is other than a cyclohexyl-$(CH_2)_2$- group;

R^{1a} is aryl and is selected from the group phenyl, naphthyl, indanyl and indenyl, each R^{1a} being substituted with 0-1 $-OR^{17}$ and 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$,

$-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$;

R^{1b} is heteroaryl and is selected from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-onyl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b}; and,

R^{1c} is heterocyclyl and is a saturated or partially saturated heteroaryl, each heterocyclyl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{13a}$, SH, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-OC(O)R^{14b}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-NR^{13a}R^{16a}$, and $-CONR^{13a}R^{16a}$ and each heterocyclyl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b} and wherein any sulfur atom is optionally monooxidized or dioxidized.

[5r] In another even more preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

X is selected from the group O, $S(O)_n$ and a bond;

n is 0, 1 or 2;

R^1 is selected from the group C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{3-8} cycloalkyl;

R^1 is substituted with a C_{3-6} cycloalkyl group, wherein 0-1 carbon atoms in the C_{4-6} cycloalkyl group is replaced by a group selected from the group -O-, $-S(O)_n-$, and $-NR^{13a}-$;

R^1 is also substituted with 0-2 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, CF_3, CF_2CF_3, $-OR^{13a}$, $-NR^{13a}R^{16a}$, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{3-6} cycloalkyl which is substituted with 0-1 R^9 and in which 0-1 carbons of C_{4-8} cycloalkyl is replaced by -O-;

R^{1a} is aryl and is selected from the group phenyl and indanyl, each R^{1a} being substituted with 0-1 $-OR^{17}$ and 0-5 substituents independently selected at each occurrence from the group C_{1-4} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, C_{1-4} haloalkyl, -CN, $-S(O)_nR^{18}$, $-COR^{17}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$;

R^{1b} is heteroaryl and is selected from the group pyridyl, pyrimidinyl, furanyl, thienyl, imidazolyl, thiazolyl, pyrrolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, and indazolyl, each heteroaryl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-4} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, CF_3, -CN, $-OR^{17}$, $-S(O)_mR^{18}$, $-COR^{17}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^2 is selected from the group C_{1-4} alkyl, C_{2-4} alkenyl, and C_{2-4} alkynyl and is substituted with 0-1 substituents selected from the group -CN, OH, Cl, F, and C_{1-4} alkoxy;

R^7 and R^8 are independently selected from the group H, Br, Cl, F, -CN, C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{1-4} alkoxy, NH_2, C_{1-4} alkylamino, and $(C_{1-4}$ alkyl$)_2$-amino;

R^9 is independently selected at each occurrence from the group H, C_{1-4} alkyl and C_{3-8} cycloalkyl;

R^{13} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{3-6} cycloalkyl-C_{1-2} alkyl, aryl(C_{1-2} alkyl)-, and heteroaryl(C_{1-2} alkyl)-;

R^{13a} and R^{16a} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{14} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{3-6} cycloalkyl-C_{1-2} alkyl, aryl(C_{1-2} alkyl)-, and heteroaryl(C_{1-2} alkyl)-;

R^{14a} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{3-6} cycloalkyl-C_{1-2} alkyl;

R^{14b} is selected from the group C_{1-4} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-2} alkyl;

R^{15} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, phenyl and benzyl, each phenyl or benzyl being substituted on the aryl moiety with 0-3 groups chosen from the group C_{1-4} alkyl, Br, Cl, F, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{15a} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{17}, R^{18} and R^{19} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{1-4} haloalkyl;

alternatively, in an $NR^{17}R^{19}$ moiety, R^{17} and R^{19} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

R^{17a} and R^{19a} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and C_{1-4} haloalkyl;

aryl is phenyl substituted with 1-4 substituents independently selected at each occurrence from the group C_{1-4} alkyl, C_{3-6} cycloalkyl, $-OR^{17}$, Br, Cl, F, C_{1-4} haloalkyl, -CN, $-S(O)_nR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-NR^{15}COR^{17}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$; and,

heteroaryl is independently selected at each occurence from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-on-yl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted 1-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F,

C_{1-4} haloalkyl, -CN, $-OR^{17}$, $-S(O)_mR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15}, CO_2R^{14a}, COR^{14a} and SO_2R^{14a}.

[5s] In another still more preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

X is selected from the group O, S and a bond

R^1 is C_{1-6} alkyl;

R^1 is substituted with a C_{3-6} cycloalkyl, wherein one carbon atom in the C_{4-6} cycloalkyl is replaced by a group selected from the group $-O-$, $-S(O)_n-$, and $-NR^{13a}-$;

R^1 is also substituted with 0-2 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, F, CF_3, $-OR^{13a}$, $-NR^{13a}R^{16a}$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, and C_{3-6} cycloalkyl which is substituted with 0-1 CH_3 and in which 0-1 carbons of C_{4-8} cycloalkyl is replaced by $-O-$;

provided that R^1 is other than a cyclohexyl-$(CH_2)_2$- group;

R^{1a} is aryl and is phenyl substituted with 0-1 substituents selected from OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, and OCF_3, and 0-3 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, Br, Cl, F, CF_3, -CN, SCH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$;

R^{1b} is heteroaryl and is selected from the group furanyl, thienyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, and indazolyl, each

heteroaryl being substituted on 0-3 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group CH_3, CO_2CH_3, $COCH_3$ and SO_2CH_3;

R^2 is selected from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, and $CH_2CH_2CH_3$;

R^7 and R^8 are independently selected from the group H, CH_3, CH_2CH_3, $CH(CH_3)_2$, and $CH_2CH_2CH_3$;

aryl is phenyl substituted with 2-4 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$; and,

heteroaryl is independently selected at each occurence from the group pyridyl, indolyl, benzothienyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, and benzoxazolin-2-on-yl, each heteroaryl being substituted on 2-4 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group CH_3, CO_2CH_3, $COCH_3$ and SO_2CH_3.

[5t] In another further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

R^1 is (cyclopropyl)C_1 alkyl or (cyclobutyl)C_1 alkyl;

R^1 is substituted with 1-2 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, $-(CH_2)_3CH_3$, $-CH=CH_2$, $-CH=CH(CH_3)$, $-CH\equiv CH$, $-CH\equiv C(CH_3)$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, F, CF_3, cyclopropyl, CH_3-cyclopropyl, cyclobutyl, CH_3-cyclobutyl, cyclopentyl, CH_3-cyclopentyl;

R^{1a} is phenyl substituted with 0-1 substituents selected from OCH_3, OCH_2CH_3, and OCF_3, and 0-2 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, Br, Cl, F, CF_3, -CN, and SCH_3;

R^{1b} is heteroaryl and is selected from the group furanyl, thienyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, triazolyl, and tetrazolyl, each heteroaryl being substituted on 0-3 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, OCH_3, OCH_2CH_3, OCF_3, Br, Cl, F, CF_3, -CN, and SCH_3 and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group CH_3, CO_2CH_3, $COCH_3$ and SO_2CH_3;

R^2 is selected from the group CH_3, CH_2CH_3, and $CH(CH_3)_2$;

R^7 and R^8 are independently selected from the group H and CH_3;

aryl is phenyl substituted with 2-4 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3,

SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$; and,

heteroaryl is pyridyl substituted on 2-4 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, CF_3, -CN, SCH_3, SO_2CH_3, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, $-C(O)NHCH_3$, and $-C(O)N(CH_3)_2$.

[5u] In another even further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

R^1 is (cyclopropyl)C_1 alkyl or (cyclobutyl)C_1 alkyl;

R^1 is substituted with 1-2 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, $-(CH_2)_3CH_3$, $-CH=CH_2$, $-CH=CH(CH_3)$, $-CH\equiv CH$, $-CH\equiv C(CH_3)$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, F, CF_3, cyclopropyl, and CH_3-cyclopropyl;

R^{1a} is phenyl substituted with 0-2 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, Br, Cl, F, CF_3, -CN, and SCH_3;

R^{1b} is heteroaryl and is selected from the group furanyl, thienyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, and pyrazolyl, each heteroaryl being substituted on 0-3 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, OCH_3, OCH_2CH_3, OCF_3, Br, Cl, F, CF_3, -CN, and SCH_3.

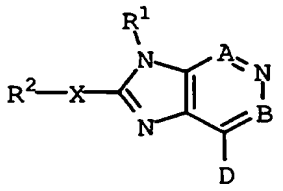
[5v] In another further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

D is phenyl substituted with 2-4 substituents independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, and CF_3.

[5w] In another further preferred embodiment, the present invention provides a novel compound of formula Id, wherein:

D is pyridyl substituted on 2-4 carbon atoms with a substituent independently selected at each occurrence from the group CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH_2CH_3$, cyclopropyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, OCF_3, Br, Cl, F, and CF_3.

[6] In a second embodiment, the present invention provides a novel method of treating affective disorder, anxiety, depression, headache, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, epilepsy, stroke, ulcers, amyotrophic lateral sclerosis, hypoglycemia or a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, in mammals, comprising: administering to the mammal a therapeutically effective amount of a compound of formula (I):



(I)

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

A is N or C-R^7;

B is N or C-R^8;

D is an aryl or heteroaryl group attached through an unsaturated carbon atom;

X is selected from the group CH-R^9, N-R^{10}, O, $S(O)_n$ and a bond;

n is 0, 1 or 2;

R^1 is selected from the group C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-8} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-4} alkoxy-C_{1-4} alkyl, $-SO_2-C_{1-10}$ alkyl, $-SO_2-R^{1a}$, and $-SO_2-R^{1b}$;

R^1 is substituted with 0-1 substituents selected from the group -CN, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-CO_2R^{13a}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-CONR^{13a}R^{16a}$, 1-morpholinyl, 1-piperidinyl, 1-piperazinyl, and C_{3-8} cycloalkyl, wherein 0-1 carbon atoms in the C_{4-8} cycloalkyl is replaced by a group selected from the group -O-, $-S(O)_n-$, $-NR^{13a}-$, $-NCO_2R^{14b}-$, $-NCOR^{14b}-$ and $-NSO_2R^{14b}-$, and wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^1 is also substituted with 0-3 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, R^{1c}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, I, C_{1-4} haloalkyl, $-OR^{13a}$, $-NR^{13a}R^{16a}$, C_{1-4} alkoxy-C_{1-4} alkyl, and C_{3-8} cycloalkyl which is substituted with 0-1 R^9 and in which 0-1 carbons of C_{4-8} cycloalkyl is replaced by -O-;

R^{1a} is aryl and is selected from the group phenyl, naphthyl, indanyl and indenyl, each R^{1a} being substituted with 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$;

R^{1b} is heteroaryl and is selected from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-onyl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^{1c} is heterocyclyl and is a saturated or partially saturated heteroaryl, each heterocyclyl being substituted on 0-4

carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{13a}$, SH, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-OC(O)R^{14b}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-NR^{13a}R^{16a}$, and $-CONR^{13a}R^{16a}$ and each heterocyclyl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b} and wherein any sulfur atom is optionally monooxidized or dioxidized;

R^2 is selected from the group C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{2-4} alkenyl, and C_{2-4} alkynyl and is substituted with 0-3 substituents selected from the group -CN, hydroxy, halo and C_{1-4} alkoxy;

alternatively R^2, in the case where X is a bond, is selected from the group -CN, CF_3 and C_2F_5;

R^7 and R^8 are independently selected at each occurrence from the group H, Br, Cl, F, I, -CN, C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, $(C_{1-4}$ alkyl$)_2$amino and phenyl, each phenyl is substituted with 0-3 groups selected from the group C_{1-7} alkyl, C_{3-8} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkyl sulfinyl, C_{1-4} alkylsulfonyl, C_{1-6} alkylamino and $(C_{1-4}$ alkyl$)_2$amino;

R^9 and R^{10} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-6} cycloalkyl-C_{1-4} alkyl and C_{3-8} cycloalkyl;

R^{13} is selected from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, aryl, aryl$(C_{1-4}$ alkyl$)$-, heteroaryl and heteroaryl$(C_{1-4}$ alkyl$)$-;

R^{13a} and R^{16a} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{14} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, aryl, aryl(C_{1-4} alkyl)-, heteroaryl and heteroaryl(C_{1-4} alkyl)- and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy C_{1-4} haloalkoxy, and dimethylamino;

R^{14a} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{14b} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{15} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, phenyl and benzyl, each phenyl or benzyl being substituted on the aryl moiety with 0-3 groups chosen from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{15a} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{17} is selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2}

alkoxy-C_{1-2} alkyl, C_{1-4} haloalkyl, $R^{14}S(O)_n$-C_{1-4} alkyl, and $R^{17b}R^{19b}N$-C_{2-4} alkyl;

R^{18} and R^{19} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{1-4} haloalkyl;

alternatively, in an $NR^{17}R^{19}$ moiety, R^{17} and R^{19} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

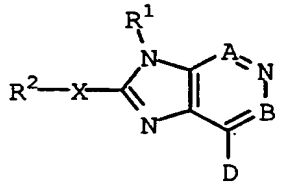
alternatively, in an $NR^{17b}R^{19b}$ moiety, R^{17b} and R^{19b} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

R^{17a} and R^{19a} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and C_{1-4} haloalkyl;

aryl is independently selected at each occurrence from the group phenyl, naphthyl, indanyl and indenyl, each aryl being substituted with 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, methylenedioxy, C_{1-4} alkoxy-C_{1-4} alkoxy, $-OR^{17}$, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, $-NO_2$, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and up to 1 phenyl, each phenyl substituent being substituted with 0-4 substituents selected from the group C_{1-3} alkyl, C_{1-3} alkoxy, Br, Cl, F, I, -CN, dimethylamino, CF_3, C_2F_5, OCF_3, SO_2Me and acetyl; and,

heteroaryl is independently selected at each occurence from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-on-yl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15}, CO_2R^{14a}, COR^{14a} and SO_2R^{14a}.

[7] In a third embodiment, the present invention provides a novel pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula (I):



(I)

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

A is N or C-R^7;

B is N or C-R^8;

D is an aryl or heteroaryl group attached through an unsaturated carbon atom;

X is selected from the group CH-R^9, N-R^{10}, O, $S(O)_n$ and a bond;

n is 0, 1 or 2;

R^1 is selected from the group C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-8} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-4} alkoxy-C_{1-4} alkyl, $-SO_2-C_{1-10}$ alkyl, $-SO_2-R^{1a}$, and $-SO_2-R^{1b}$;

R^1 is substituted with 0-1 substituents selected from the group -CN, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-CO_2R^{13a}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-CONR^{13a}R^{16a}$, 1-morpholinyl, 1-piperidinyl, 1-piperazinyl, and C_{3-8} cycloalkyl, wherein 0-1 carbon atoms in the C_{4-8} cycloalkyl is replaced by a group selected from the group -O-, $-S(O)_n-$, $-NR^{13a}-$, $-NCO_2R^{14b}-$, $-NCOR^{14b}-$ and $-NSO_2R^{14b}-$, and wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^1 is also substituted with 0-3 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, R^{1c}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, I, C_{1-4} haloalkyl, $-OR^{13a}$, $-NR^{13a}R^{16a}$, C_{1-4} alkoxy-C_{1-4} alkyl, and C_{3-8} cycloalkyl which is substituted with 0-1 R^9 and in which 0-1 carbons of C_{4-8} cycloalkyl is replaced by -O-;

R^{1a} is aryl and is selected from the group phenyl, naphthyl, indanyl and indenyl, each R^{1a} being substituted with 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_nR^{18}$, $-COR^{17}$,

$-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$;

R^{1b} is heteroaryl and is selected from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-onyl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^{1c} is heterocyclyl and is a saturated or partially saturated heteroaryl, each heterocyclyl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{13a}$, SH, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-OC(O)R^{14b}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-NR^{13a}R^{16a}$, and $-CONR^{13a}R^{16a}$ and each heterocyclyl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b} and wherein any sulfur atom is optionally monooxidized or dioxidized;

R^2 is selected from the group C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{2-4} alkenyl, and C_{2-4} alkynyl and is substituted with 0-3

substituents selected from the group -CN, hydroxy, halo and C_{1-4} alkoxy;

alternatively R^2, in the case where X is a bond, is selected from the group -CN, CF_3 and C_2F_5;

R^7 and R^8 are independently selected at each occurrence from the group H, Br, Cl, F, I, -CN, C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, $(C_{1-4}$ alkyl$)_2$amino and phenyl, each phenyl is substituted with 0-3 groups selected from the group C_{1-7} alkyl, C_{3-8} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkyl sulfinyl, C_{1-4} alkylsulfonyl, C_{1-6} alkylamino and $(C_{1-4}$ alkyl$)_2$amino;

R^9 and R^{10} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-6} cycloalkyl-C_{1-4} alkyl and C_{3-8} cycloalkyl;

R^{13} is selected from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, aryl, aryl$(C_{1-4}$ alkyl$)$-, heteroaryl and heteroaryl$(C_{1-4}$ alkyl$)$-;

R^{13a} and R^{16a} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{14} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, aryl, aryl$(C_{1-4}$ alkyl$)$-, heteroaryl and heteroaryl$(C_{1-4}$ alkyl$)$- and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4}

haloalkyl, nitro, C_{1-4} alkoxy C_{1-4} haloalkoxy, and dimethylamino;

R^{14a} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{14b} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{15} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, phenyl and benzyl, each phenyl or benzyl being substituted on the aryl moiety with 0-3 groups chosen from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{15a} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{17} is selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{1-4} haloalkyl, $R^{14}S(O)_n$-C_{1-4} alkyl, and $R^{17b}R^{19b}N$-C_{2-4} alkyl;

R^{18} and R^{19} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{1-4} haloalkyl;

alternatively, in an $NR^{17}R^{19}$ moiety, R^{17} and R^{19} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted

with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

alternatively, in an $NR^{17b}R^{19b}$ moiety, R^{17b} and R^{19b} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

R^{17a} and R^{19a} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and C_{1-4} haloalkyl;

aryl is independently selected at each occurrence from the group phenyl, naphthyl, indanyl and indenyl, each aryl being substituted with 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, methylenedioxy, C_{1-4} alkoxy-C_{1-4} alkoxy, $-OR^{17}$, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, $-NO_2$, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and up to 1 phenyl, each phenyl substituent being substituted with 0-4 substituents selected from the group C_{1-3} alkyl, C_{1-3} alkoxy, Br, Cl, F, I, -CN, dimethylamino, CF_3, C_2F_5, OCF_3, SO_2Me and acetyl; and,

heteroaryl is independently selected at each occurence from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-on-yl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted 0-4 carbon atoms with a

substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15}, CO_2R^{14a}, COR^{14a} and SO_2R^{14a}.

In another preferred embodiment, R^1 is other than a cyclohexyl-$(CH_2)_{1, 2, 3, 4, 5, 6, 7, 8, 9, or 10}$- group;

In another preferred embodiment, R^1 is other than an aryl-$(CH_2)_{1, 2, 3, 4, 5, 6, 7, 8, 9, or 10}$- group, wherein the aryl group is substituted or unsubstituted;

In another preferred embodiment, R^1 is other than a heteroaryl-$(CH_2)_{1, 2, 3, 4, 5, 6, 7, 8, 9, or 10}$- group, wherein the heteroaryl group is substituted or unsubstituted;

In another preferred embodiment, R^1 is other than a heterocyclyl-$(CH_2)_{1, 2, 3, 4, 5, 6, 7, 8, 9, or 10}$- group, wherein the heterocyclyl group is substituted or unsubstituted;

In another preferred embodiment, when D is imidazole or triazole, R^1 is other than unsubstituted $C_{1, 2, 3, 4, 5, 6, 7, 8, 9, or 10}$ linear or branched alkyl or $C_{3, 4, 5, 6, 7, or 8}$ cycloalkyl.

In another preferred embodiment, R^{1a} is not substituted with OR^{17}.

In fourth embodiment, the present invention provides intermediate compounds useful in preparation of the CRF antagonist compounds and processes for making those intermediates, as described in the following description and claims.

In a fifth embodiment, the present invention provides CRF antagonist compounds and labelled derivatives thereof as standards and reagents in determining the ability of a potential pharmaceutical to bind to the CRF receptor.

DEFINITIONS

The compounds herein described may have asymmetric centers. Compounds of the present invention containing an asymmetrically substituted atom may be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of the compounds of the present invention are described and may be isolated as a mixture of isomers or as separated isomeric forms. All chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomeric form is specifically indicated. All processes used to prepare compounds of the present invention and intermediates made therein are considered to be part of the present invention.

The term "substituted," as used herein, means that any one or more hydrogens on the designated atom is replaced with

a selection from the indicated group, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a substitent is keto (i.e., =O), then 2 hydrogens on the atom are replaced. Keto substituents are not present on aromatic moieties.

The present invention is intended to include all isotopes of atoms occurring in the present compounds. Isotopes include those atoms having the same atomic number but different mass numbers. By way of general example and without limitation, isotopes of hydrogen include tritium and deuterium. Isotopes of carbon include C-13 and C-14.

When any variable (e.g., R^6) occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-2 R^6, then said group may optionally be substituted with up to two R^6 groups and R^6 at each occurrence is selected independently from the definition of R^6. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent may be bonded to any atom on the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound of a given formula, then such substituent may be bonded via any atom in such substituent. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

As used herein, "alkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms. Examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, and s-pentyl. "Haloalkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms, substituted with 1 or more halogen (for example $-C_vF_w$ where v = 1 to 3 and w =

1 to (2v+1)). Examples of haloalkyl include, but are not limited to, trifluoromethyl, trichloromethyl, pentafluoroethyl, and pentachloroethyl. "Alkoxy" represents an alkyl group as defined above with the indicated number of carbon atoms attached through an oxygen bridge. Examples of alkoxy include, but are not limited to, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy, n-pentoxy, and s-pentoxy. "Cycloalkyl" is intended to include saturated ring groups, such as cyclopropyl, cyclobutyl, or cyclopentyl. Alkenyl" is intended to include hydrocarbon chains of either a straight or branched configuration and one or more unsaturated carbon-carbon bonds which may occur in any stable point along the chain, such as ethenyl and propenyl. "Alkynyl" is intended to include hydrocarbon chains of either a straight or branched configuration and one or more triple carbon-carbon bonds which may occur in any stable point along the chain, such as ethynyl and propynyl.

"Halo" or "halogen" as used herein refers to fluoro, chloro, bromo, and iodo; and "counter-ion" is used to represent a small, negatively charged species such as chloride, bromide, hydroxide, acetate, sulfate, and the like.

"Halo" or "halogen" as used herein refers to fluoro, chloro, bromo, and iodo; and "counterion" is used to represent a small, negatively charged species such as chloride, bromide, hydroxide, acetate, and sulfate.

As used herein, "carbocycle" or "carbocyclic residue" is intended to mean any stable 3- to 7-membered monocyclic or bicyclic or 7-to 13-membered bicyclic or tricyclic, any of which may be saturated, partially unsaturated, or aromatic. Examples of such carbocycles include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantyl, cyclooctyl, [3.3.0]bicyclooctane, [4.3.0]bicyclononane, [4.4.0]bicyclodecane, [2.2.2]bicyclooctane, fluorenyl, phenyl, naphthyl, indanyl, adamantyl, and tetrahydronaphthyl.

As used herein, the term "heterocycle" or "heterocyclic system" is intended to mean a stable 5-to 7-membered monocyclic or bicyclic or 7-to 10-membered bicyclic

heterocyclic ring which is saturated partially unsaturated or unsaturated (aromatic), and which consists of carbon atoms and from 1 to 4 heteroatoms independently selected from the group consisting of N, O and S and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. The nitrogen and sulfur heteroatoms may optionally be oxidized. The heterocyclic ring may be attached to its pendant group at any heteroatom or carbon atom which results in a stable structure. The heterocyclic rings described herein may be substituted on carbon or on a nitrogen atom if the resulting compound is stable. A nitrogen in the heterocycle may optionally be quaternized. It is preferred that when the total number of S and O atoms in the heterocycle exceeds 1, then these heteroatoms are not adjacent to one another. It is preferred that the total number of S and O atoms in the heterocycle is not more than 1. As used herein, the term "aromatic heterocyclic system" is intended to mean a stable 5-to 7-membered monocyclic or bicyclic or 7-to 10-membered bicyclic heterocyclic aromatic ring which consists of carbon atoms and from 1 to 4 heterotams independently selected from the group consisting of N, O and S. It is preferred that the total number of S and O atoms in the aromatic heterocycle is not more than 1.

Examples of heterocycles include, but are not limited to, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazolinyl, carbazolyl, 4a*H*-carbazolyl, carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2*H*,6*H*-1,5,2-dithiazinyl, dihydrofuro[2,3-*b*]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, 1*H*-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, 3H-indolyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl,

oxazolidinyl, pyrimidinyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, 2H-pyrrolyl, pyrrolyl, quinazolinyl, quinolinyl, 4*H*-quinolizinyl, quinoxalinyl, quinuclidinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, 6*H*-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, and xanthenyl. Preferred heterocycles include, but are not limited to, pyridinyl, furanyl, thienyl, pyrrolyl, pyrazolyl, pyrrolidinyl, imidazolyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, and isatinoyl. Also included are fused ring and spiro compounds containing, for example, the above heterocycles.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; and alkali or organic salts of acidic residues such as carboxylic acids. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed,

for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, and nitric; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, and isethionic.

The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, PA, 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

"Prodrugs" are intended to include any covalently bonded carriers which release the active parent drug according to formula (I) *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs of a compound of formula (I) are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound. Prodrugs include compounds of formula (I) wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug or compound of formula (I) is administered to a mammalian subject, cleaves to form a free hydroxyl, free amino, or free sulfhydryl group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol and amine

functional groups in the compounds of formula (I), and the like.

"Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

"Substituted" is intended to indicate that one or more hydrogens on the atom indicated in the expression using "substituted" is replaced with a selection from the indicated group(s), provided that the indicated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a substituent is keto (i.e., =O) group, then 2 hydrogens on the atom are replaced.

"Therapeutically effective amount" is intended to include an amount of a compound of the present invention or an amount of the combination of compounds claimed effective to inhibit HIV infection or treat the symptoms of HIV infection in a host. The combination of compounds is preferably a synergistic combination. Synergy, as described for example by Chou and Talalay, Adv. Enzyme Regul. 22:27-55 (1984), occurs when the effect (in this case, inhibition of HIV replication) of the compounds when administered in combination is greater than the additive effect of the compounds when administered alone as a single agent. In general, a synergistic effect is most clearly demonstrated at suboptimal concentrations of the compounds. Synergy can be in terms of lower cytotoxicity, increased antiviral effect, or some other beneficial effect of the combination compared with the individual components.

Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds. A stable compound or stable structure is meant to imply a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an effective therapeutic agent.

The term "therapeutically effective amount" of a compound of this invention means an amount effective to antagonize

abnormal level of CRF or treat the symptoms of affective disorder, anxiety or depression in a host.

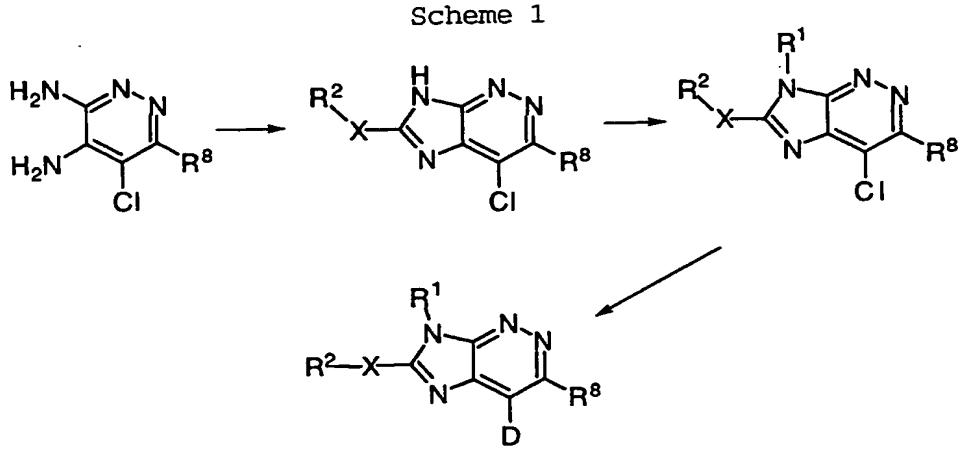
SYNTHESIS

The compounds of the present invention can be prepared in a number of ways well known to one skilled in the art of organic synthesis. The compounds of the present invention can be synthesized using the methods described below, together with synthetic methods known in the art of synthetic organic chemistry, or variations thereon as appreciated by those skilled in the art. Preferred methods include but are not limited to those methods described below. Each of the references cited below are hereby incorporated herein by reference.

The following abbreviations are used herein:

AcOH	acetic acid
t-BuOK	potassium *tert*-butoxide
DEAD	diethyl azodicarboxylate
DMSO	dimethyl sulfoxide
EtOAc	ethyl acetate
EtOH	ethanol
NaHMDS	sodium bis(trimethylsilyl)amide
PPh_3	triphenylphosphine
THF	tetrahydrofuran
TLC	thin layer chromatography

Scheme 1

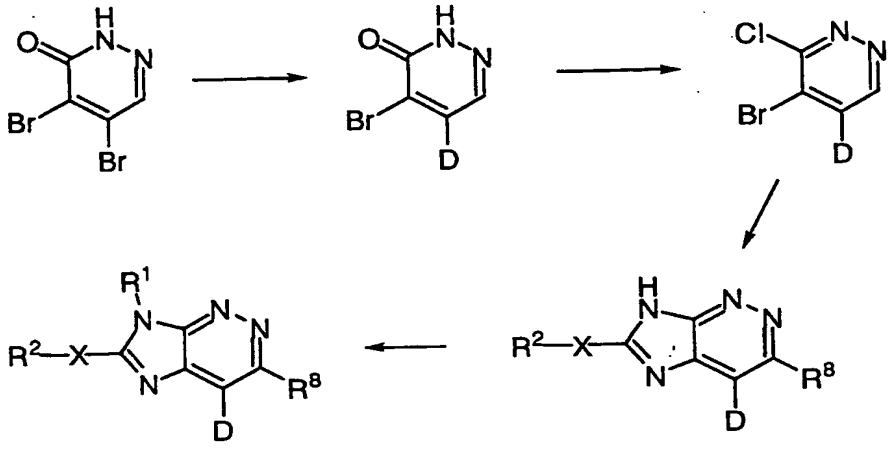


(Ia)

The compounds of this invention of formula (Ia) may be prepared using the methods shown in Scheme 1. In this procedure the 5-chloro-3,4-diaminopyridazine precursor may be cyclized to the desired imidazopyridiazines using orthoesters (for R^2-X- = H, alkyl, alkoxy, etc.), orthocarbonates, carboxylic acids, carboxylic acid esters, alkyl imidates and other reagents appropriate to the product desired, and reaction conditions known to those skilled in the art of organic synthesis. The synthesis of the starting material where R^8=H, and the chemistry thereof has been described by Kurashi and Castle (*J. Het. Chem.* **1964**, *1*, 42).

The imidazolepyridazine may then be N-alkylated using, for example, base promoted conditions (e.g., NaHMDS/R^1-LG, where LG = halide, sulfonate, or other appropriate leaving group) or Mitsunobu reaction conditions (e.g., DEAD/PPh_3/R^1-OH). The compounds of formula (Ia) are then formed by cross coupling with an appropriate arylboronic acid, arylstannane, or arylzinc reagent under known conditions. In the case where R^1 is a protecting group such as benzyl, p-methoxybenzyl, or tetrahydropyranyl (*J. Het. Chem.* **1968**, *5*, 13), the group may be removed and N-alkylation at this point gives compounds of formula (Ia).

Scheme 2



(Ia)

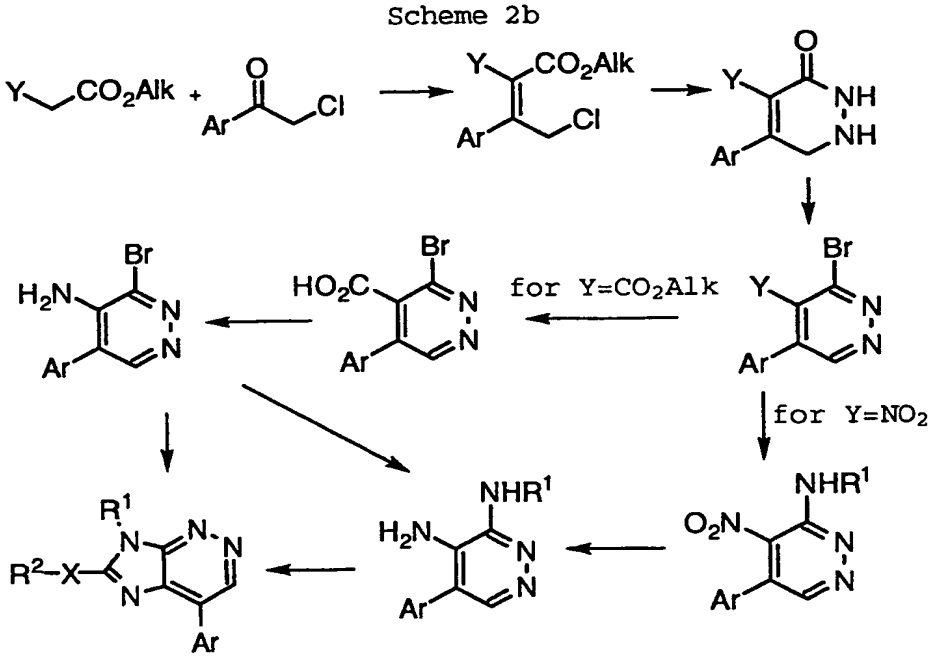
Compounds of formula (Ia) may also be prepared via the method outlined in Scheme 2. Commercially available 4,5-dibromo-pyridazin-3-one is N and/or O benzylated then cross coupled in, for example, a Suzuki reaction (D-$B(OH)_2/Pd(PPh_3)_4/Na_2CO_3$) followed by deprotection. Chlorination using, for example, $POCl_3$ gives a chloro-pyridazine which may then be reacted for example, with an amidine. N-alkylation of the resulting bicyclic compound using the methods described above affords the desired compounds of formula (Ia).

Compounds of formula (Ia) may also be prepared via the method outlined in Scheme 2b. In this procedure, a 2-chloroacetophenone is condensed with a dialkyl malonate (e.g., $TiCl_4/CCl_4$/pyridine/THF) or nitroacetate. The product from this reaction is treated with hydrazine to give an intermediate which is oxidized using, for example, DDQ or NBS to give the pyridazinone intermediate. Chlorination (or bromination) using $POCl_3$ (or $POBr_3$) affords a chloro- (or bromo-) pyridazine intermediate.

This intermediate, where Y = ester in Scheme 2b, may now be converted to the acid (e.g., $LiOH/H_2O$/MeOH/THF) and then subjected to conditions such as the Curtius reaction or modifications thereof (e.g., DPPA, Et_3N, t-BuOH; TFA/CH_2Cl_2),

which transform the acid to an amino group. Substitution of the halide with an appropriate amine using, for example, nucleophilic substitution or cross-coupling reactions, affords an intermediate which can then be converted to the desired imidazopyridiazines (Ia) by cyclization using orthoesters (for R^2-X- = H, alkyl, alkoxy, etc.), orthocarbonates, carboxylic acids, carboxylic acid esters, alkyl imidates and other reagents appropriate to the product desired, and reaction conditions known to those skilled in the art of organic synthesis.

Scheme 2b

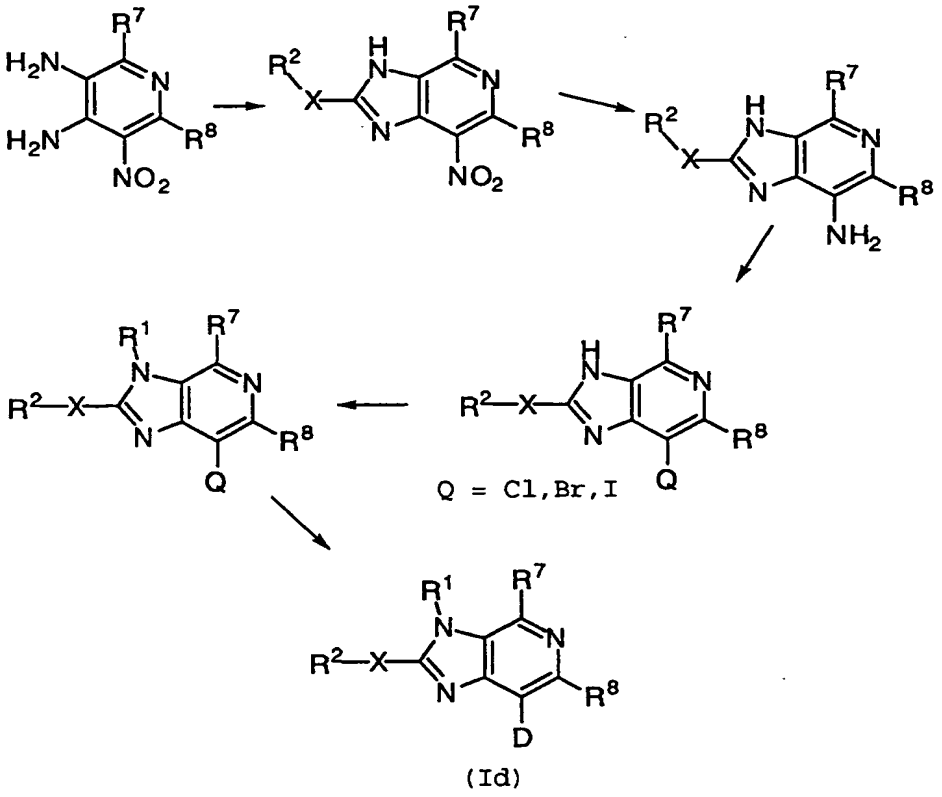


(Ia)

The intermediate where Y = NO_2 in Scheme 2b may be treated with an appropriate amine using, for example, nucleophilic substitution conditions. Reduction of the nitro group to the amine (e.g., Fe/AcOH or sodium dithionite/water/EtOH) affords an intermediate which can then be converted to the desired imidazopyridiazines (Ia) by cyclization using orthoesters (for R^2-X- = H, alkyl, alkoxy, etc.), orthocarbonates, carboxylic acids, carboxylic acid esters, alkyl imidates and other reagents appropriate to the

product desired, and reaction conditions known to those skilled in the art of organic synthesis.

Scheme 3

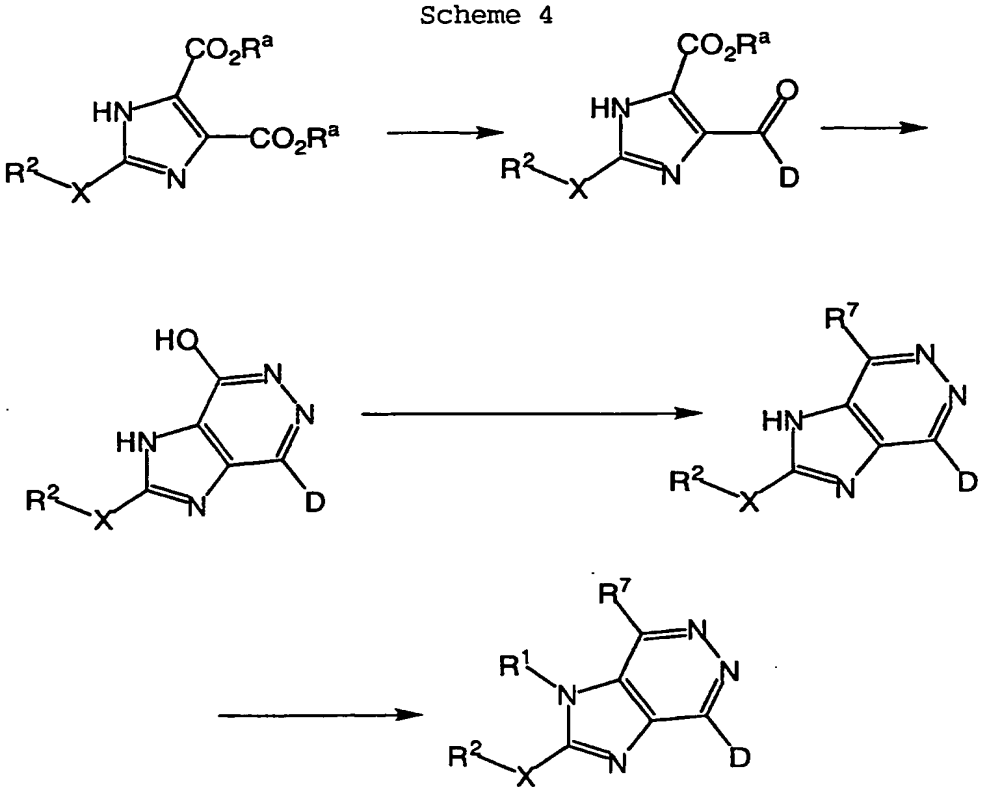


(Id)

The compounds of this invention of formula (Id) may be prepared using the methods shown in Scheme 3. In this procedure, the 3,4-diamino-5-nitropyridine precursor may be cyclized to the desired imidazopyridines using orthoesters (for R^2-X- = H, alkyl, alkoxy, etc.), orthocarbonates, carboxylic acids, carboxylic acid esters, alkyl imidates and other reagents appropriate to the product desired, and reaction conditions known to those skilled in the art of organic synthesis. The synthesis of the precursor where R^7 and R^8=H, and the chemistry thereof has been described by Graboyes and Day (*J. Am. Chem. Soc.* **1957**, *79*, 6421).

Reduction of the nitro group using, for example, stannous chloride, provides the amino compound. Conversion of the amino group to a chloride, bromide or iodide may now be effected via diazotization of the amine followed by displacement with halogen anion. The halide compounds may then be N-alkylated using, for example, base promoted conditions (e.g., NaHMDS/R^1-LG, where LG = halide, sulfonate, or other appropriate leaving group) or Mitsunobu reaction conditions (e.g., DEAD/PPh_3/R^1-OH). Cross coupling with an appropriate arylboronic acid, arylstannane, or arylzinc reagent under known conditions to yield compounds of formula (Id). In the case where R^1 is a protecting group, the group may now be removed and N-alkylation at this point gives compounds of formula (Id).

Scheme 4



(Ib)

Compounds of Formula (Ib) may be prepared, using the procedures outlined in Scheme 4. The starting material (where Ra is lower alkyl, X and R2 are defined above) may be treated with a compound of the formula D-M (where M = Li, Na, MgBr, MgCl, ZnCl, $CeCl_2$ and D is defined above) in the presence of an inert solvent at reaction temperatures ranging from -80°C to 250°C to provide the keto-imidazole. Inert solvents may include, but are not limited to, dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane) or aromatic hydrocarbons (preferably benzene or toluene).

The imidazolepyridazine can then be formed by reaction with hydrazine in an inert solvent. Inert solvents may include, but are not limited to, alkyl alcohols (1 to 6 carbons), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from -80 to 120°C.

The hydroxypyridazine may then be treated with a halogenating agent to give halo derivatives which may be isolated or prepared in situ. Halogenating agents include, but are not limited to, $SOCl_2$, $POCl_3$, PCl_3, PCl_5, $POBr_3$, PBr_3 or PBr_5. These intermediates may be treated with a compound of the Formula R^7H in the presence or absence of a base in an inert solvent. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons)(preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine), aromatic amines (preferably pyridine) or alkyl-lithiums in the presence or absence of salts or complexes of Cu, Ce, Mg, Pd, Ni, Zn, Sn. Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-

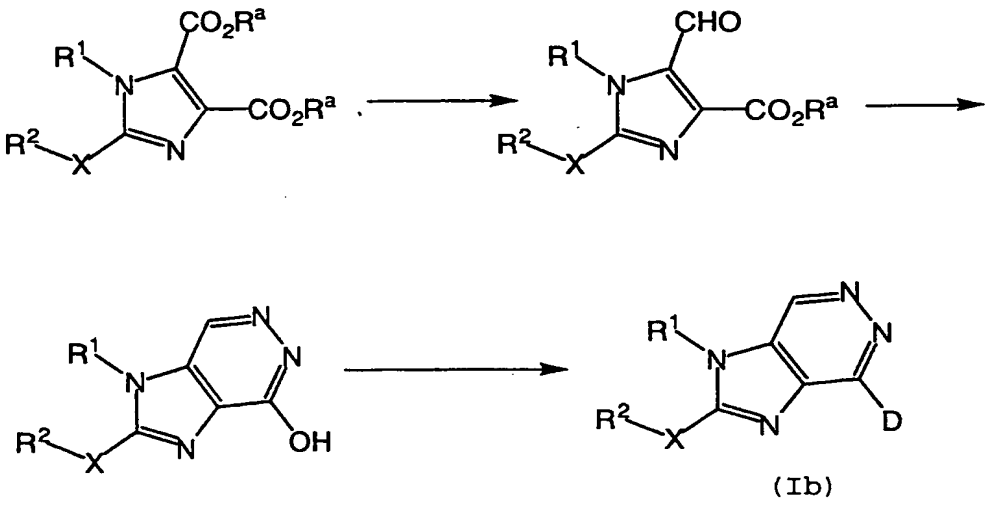
dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from -20 to 100°C.

The resulting compounds may then be reacted with an alkylating agent of the Formula R^1X (where R^1 is defined above) and X is halo, alkanesulfonyloxy, arylsulfonyloxy or haloalkane-sulfonyloxy) in the presence or absence of a base in an inert solvent to provide compounds of Formula (Id). Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons)(preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine), aromatic amines (preferably pyridine) or alkyl-lithiums in the presence or absence of salts or complexes of Cu, Ce, Mg, Pd, Ni, Zn, Sn. Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from -20 to 100°C.

Alternatively, alkylation to compounds of Formula (Ib) by treatment with a azodicarboxylate ester $R^bO_2CN{=}NCO_2R^b$ (where R^b is a lower alkyl group) and a compound of the Formula R^1OH in

the presence of a triarylphosphine (where aryl is phenyl or furyl, each optionally substituted by 0 to 3 alkyl groups) in an inert solvent. Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from -20 to 100°C.

Scheme 5



(Ib)

Compounds of Formula (Ib) may also be prepared, using the procedures outlined in Scheme 5. The starting diester may be treated with a reducing agent in inert solvent to afford an aldehyde. Reducing agents include, but are not limited to, alkali metal or alkaline earth metal borohydrides (preferably lithium or sodium borohydride), borane, dialkylboranes (such as di-isoamylborane), alkali metal aluminum hydrides (preferably lithium aluminum hydride), alkali metal

(trialkoxy)aluminum hydrides, or dialkyl aluminum hydrides (such as di-isobutylaluminum hydride). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 6 carbons), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from -80 to 100°C.

Alternatively, the aldehyde may be prepared by a two step sequence: treatment with a reducing agent in an inert solvent, followed by treatment with an oxidizing agent in an inert solvent. Reducing agents and inert solvents are defined above. Oxidizing agents include, but are not limited to, combinations of oxalyl chloride, dimethyl sulfoxide and organic bases, MnO2, KMnO4, pyridinium dichromate, pyridinium chlorochromate or combinations of SO_3 and organic bases. Organic bases include, but are not limited to, trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine).

The aldehyde may then be reacted with hydrazine in an inert solvent to form an imidazole. Inert solvents may include, but are not limited to, alkyl alcohols (1 to 6 carbons), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from -80 to 120°C.

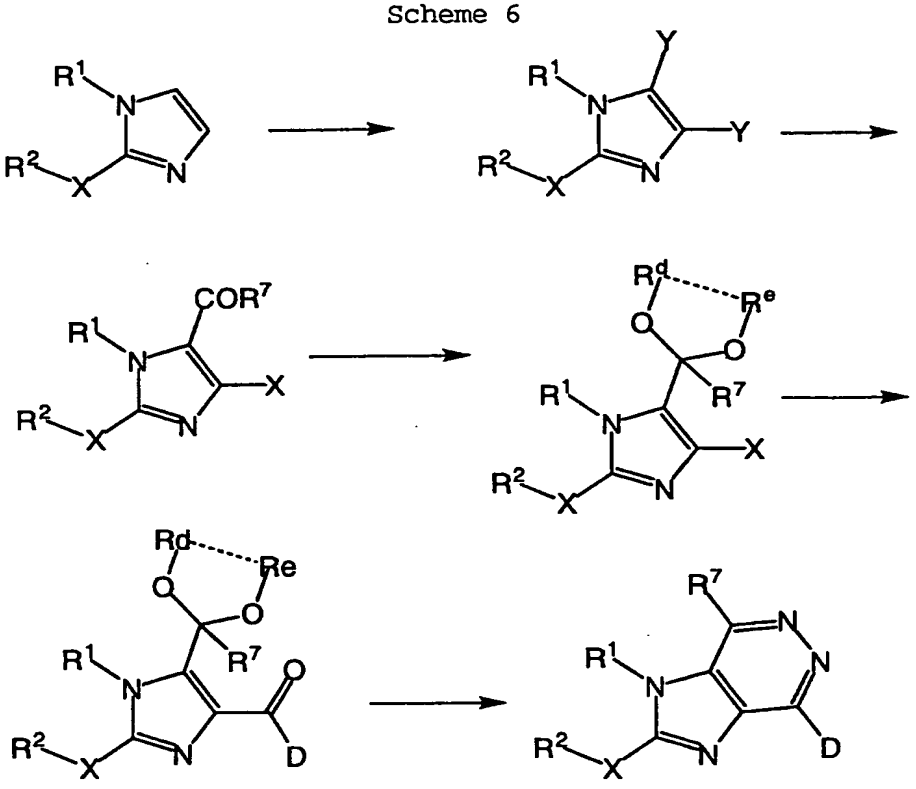
The hydroxy group may then be treated with sulfonylating agents in the presence or absence of a base to give alkanesulfonyloxy, arylsulfonyloxy or haloalkylsulfonyloxy derivatives, which may be isolated or used in situ. Sulfonylating agents include, but are not limited to, alkanesulfonyl halides or anhydrides (such as methanesulfonyl chloride or methanesulfonic acid anhydride), arylsulfonyl halides or anhydrides (such as p-toluenesulfonyl chloride or anhydride) or haloalkylsulfonyl halides or anhydrides (preferably trifluoromethanesulfonic anhydride). Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons)(preferably sodium methoxide or sodium ethoxide),

alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane).

The sulfonylated intermediates may then be reacted with compounds of the formula D-B(OH)2 in the presence of salts or complexes of Pd, Ni, or Sn, in the presence or absence of a base in an inert solvent to provide compounds of Formula (Ib). Bases may include, but are not limited to, alkaline earth metal carbonates, alkaline earth metal bicarbonates, alkaline earth metal hydroxides, alkali metal carbonates, alkali metal bicarbonates, alkali metal hydroxides, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons)(preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-

methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane).

Scheme 6



(Ib)

Compounds of Formula (Ib) may also be prepared by the procedures outlined in Scheme 6. The starting imidazoles may treated with halogenating agents in an inert solvent to provide a dihalo-imidazole. Halogenating agents include, but are not limited to, $SOCl_2$, $POCl_3$, PCl_3, PCl_5, $POBr_3$, PBr_3 or PBr_5. Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic

amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane).

One halogen may be replaced via treatment with a compound of Formula R^cM (where R^c is lower alkyl and M may be Li, Na, MgBr, MgCl, ZnCl, $CeCl_2$) in an inert solvent, followed by reaction with a compound of Formula R^7-(C=O)-Y (where R^7 is defined above and Y is halogen, lower alkoxy, lower alkanoyloxy or $(R^dO)_2(P=O)O$ (where R^d is lower alkyl or phenyl)). The acyl compounds my be protected by reaction with acetal- or ketal- forming reagents (where R^d or R^e are each lower alkyl, or taken together they form a lower alkylene chain). These acetal- or ketal- forming reagents may be combinations of lower alkyl alcohols or diols and acids or trialkylorthoformates and acids. Such acids may be present in catalytic or stoichiometric amounts. Such acids include, but are not limited to, alkanoic acids of 2 to 10 carbons (preferably acetic acid), arylsulfonic acids (preferably p-toluenesulfonic acid or benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), hydrochloric acid, sulfuric acid or phosphoric acid. Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably glyme or diglyme), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or halocarbons of 1 to 10 carbons and 1 to 10 halogens (preferably chloroform). Preferred reaction temperatures range from ambient temperature to 150°C.

Moiety D may be attached by treatment with a compound of Formula R^cM (where R^c is lower alkyl and M may be Li, Na,

MgBr, MgCl, ZnCl, $CeCl_2$) in an inert solvent, followed by reaction with a compound of Formula D-(C=O)-Y (where D is defined above and Y is halogen, lower alkoxy, lower alkanoyloxy or $(R^dO)_2(P=O)O$ (where R^d is lower alkyl or phenyl)). Inert solvents may include, but are not limited to, dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), or aromatic hydrocarbons (preferably benzene or toluene).

Compounds of Formula (Ib) may finally be prepared by (a) hydrolysis with an acid, followed by (b) reaction with hydrazine in an inert solvent. Acids include, but are not limited to, alkanoic acids of 2 to 10 carbons (preferably acetic acid), arylsulfonic acids (preferably p-toluenesulfonic acid or benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), hydrochloric acid, sulfuric acid or phosphoric acid. Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably glyme or diglyme), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or halocarbons of 1 to 10 carbons and 1 to 10 halogens (preferably chloroform). Preferred reaction temperatures for steps (a) or (b) range from ambient temperature to 150°C.

If intermediates contain functional groups which are sensitive to the reaction conditions employed, these groups may be protected using methods known to those skilled in the art. These methods include, but are not limited to, those described in Protective Groups in Organic Synthesis (Greene, Wuts; 2nd ed., 1991, John Wiley & Sons, Inc.).

Other features of the invention will become apparent in the course of the following descriptions of exemplary

embodiments which are given for illustration of the invention and are not intended to be limiting thereof.

Examples

Abbreviations used in the Examples are defined as follows: "1 x" for once, "2 x" for twice, "3 x" for thrice, "°C" for degrees Celsius, "eq" for equivalent or equivalents, "g" for gram or grams, "mg" for milligram or milligrams, "mL" for milliliter or milliliters, "^{1}H" for proton, "h" for hour or hours, "M" for molar, "min" for minute or minutes, "MHz" for megahertz, "MS" for mass spectroscopy, "NMR" for nuclear magnetic resonance spectroscopy, "rt" for room temperature, "tlc" for thin layer chromatography, "v/v" for volume to volume ratio. "α", "β", "R" and "S" are stereochemical designations familiar to those skilled in the art.

Example 1

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-ethyl)propyl-imidazo[4,5-d]pyridazine

Part A: 4,5-dibromo-2-ethyl-1H-imidazole:
To a solution of 2-ethylimidazole (57.6 g, 0.6 moles) in $CHCl_3$ (700 mL) was cooled to 0- 5 °C and then added bromine (76.8 mL, 1.5 moles) dropwise over 60 mins under nitrogen atmosphere. The mixture was stirred at 5 °C for 60 mins and then at room temperature for 2 days. TLC (1:10 MeOH/CH_2Cl_2) revealed disappearence of starting material (Rf=0.25) and showed a new spot (Rf=0.45). The mixture was cooled back to 0 °C and added dropwise 2N aq. NaOH (750 mL) to dissolve the yellow solid separated from the mixture. The aq. layer was separated and extracted the organic layer with 250 mL of 2N NaOH. The combined aq. extracts was acidified to pH 8.0 using con. HCl. The cream colored solid separated was filtered, washed with water and dried in vacuum at 50 °C to afford 55.0 g of desired product (mp 149-150 °C, 36 %). ^{1}H NMR ($CDCl_3$): ∂ 1.27-1.3 (t, 3H, CH_3), 2.7-2.8 (q, 2H, CH_2). Mass spectrum (CI-NH_3): m/z 255.0 (MH^+).

Part B: 4,5-dibromo-2-ethyl-1-(1-ethyl)propyl-1H-imidazole:

A mixture of part A material (8.3 g, 0.033 moles), triphenylphosphine (9.4 g, 0.036 moles) and molecular sieves (10 g) in THF (100 mL) was cooled to 0 to - 5 °C and then added 3-pentanol (3.4 g, 0.039 moles) under nitrogen atmosphere. The mixture was stirred at 0 °C for 30 mins and then added disopropylazodicarboxylate (7.2 g, 0.033 moles) dropwise over 20 mis. The mixture was stirred at 0 °C for 2h followed by room temperature for 2 days and TLC (1:50 $MeOH/CH_2Cl_2$) revealed a new spot at Rf=0.5. The undissolved material was filtered, washed with dichloromethane and stripped off the solvent in vacuum to afford yellow liquid. The crude was purified by flash column chromatography using chloroform as eluent to afford 4.9 g (46.5 %) of colorless oil. ^1H NMR ($CDCl_3$): ∂ 0.79-0.84 (t, 6H, 2*CH_3), 1.3-1.35 (t, 3H, CH_3), 1.82-2.18 (m, 4H, 2*CH_2), 2.65-2.72 (q, 2H, CH_2), 3.95 (m, 1H, CH). Mass spectrum (CI-NH_3): m/z 325.0 (MH^+).

Part C: 4-bromo-2-ethyl-1-(1-ethyl)propyl-1H-imidazole-5-carboxaldehyde:

A solution of part B material (3.7 g, 0.0114 moles) in THF (40.0 mL) was cooled to - 78 °C under nitrogen atmosphere and then added dropwise 1.6 M n-BuLi solution in hexane (7.4 mL, 0.0119 moles) over 30 mins. The mixture was stirred at -78 °C for 1h and then added dropwise DMF (2.7 mL, 0.0342 moles) over 15 mins. The mixture was stirred at -78 °C for 60 mins and quenched with saturated NH_4Cl (10 mL) at -78 °C. TLC (1:50 $MeOH/CH_2Cl_2$) revealed a new spot at Rf=0.55 along with disappearence of starting material spot at Rf=0.5. The reaction mixture was extracted with diethyl ether (3 * 25 mL), washed with brine and dried ($MgSO_4$). The solvent was stripped off in vacuo to afford 3.6 g of yellow oil which was purified by flash column chromatography on silica gel using chloroform as eluent to afford 1.97 g (64 % yield) of colorless oil. ^1H NMR ($CDCl_3$): ∂ 0.73-0.83 (t, 6H, 2*CH_3), 1.35-1.40 (t, 3H, CH_3), 1.59-2.17 (m, 4H, 2*CH_2), 2.72-2.80 (q, 2H, CH_2), 3.95

(m, 1H, CH), 9.67 (s, 1H, CHO). Mass spectrum (CI-NH_3): m/z 275.1 (M+2H).

Part D: 4-bromo-2-ethyl-1-(1-ethyl)propyl-1H-imidazole-5-carboxaldehyde ethylene acetal:

A mixture of part C material (1.75 g, 0.0064 moles) in benzene (150 mL) was treated with ethylene glycol (1.2 mL, 0.025 moles), pyridine (0.0035 moles) and p-toluenesulfonic acid mono hydrate (0.0035 moles). The reaction mixture was heated at reflux in a 20 mL capacity Dean-Stark trap equipped apparatus for 24 h and TLC (1:50 MeOH/CH_2Cl_2) revealed a new spot at Rf=0.35 (visible under iodine). The reaction mixture was cooled to room temperature, diluted with EtOAc (50 mL), washed with 10 % sodium bicarbonate, brine and dried ($MgSO_4$). The solvent was evaporated under reduced pressure to furnish yellow oil. The crude was purified by flash column chromatography on silica gel using 25 % ethyl acetate/chloroform mixture to afford 1.96 g (97 %) white solid (mp 70-71 °C). ^1H NMR ($CDCl_3$): ∂ 0.78-0.89 (t, 6H, 2*CH_3), 1.29-1.36 (t, 3H, CH_3), 1.77-1.90 (m, 4H, 2*CH_2), 2.70-2.73 (q, 2H, CH_2), 3.98-4.3 (m, 5H, CH and 2*CH_2), 5.86 (s, 1H, CH). Mass spectrum (CI-NH_3): m/z 317.1 (M^+). Anal. calcd for $C_{13}H_{22}Br_1N_2O_2$: C, 49.22; H, 6.67; N, 8.83. Found: C, 49.43; H, 6.61; N, 8.78.

Part E: 4-(2,4-dichlorobenzoyl)-2-ethyl-1-(1-ethyl)propyl-1H-imidazole-5-carboxaldehyde:

A solution of part D material (1.08 g, 0.0034 moles) in THF (20.0 mL) was cooled to - 78 °C and then added dropwise 1.6 M n-BuLi in hexane (2.4 mL, 0.004 moles) over 15 mins under nitrogen atmosphere. The mixture was stirred at -78 °C for 2 1/2 h and then added a solution of 2,4-dichlorobenzoyl chloride (0.84 g, 0.004 moles) in THF (5.0 mL) over 15 mins. The mixture was stirred at -78 °C for 6 h followed by room temperature overnight and TLC (30:70 EtOAc/hexane) showed a new spot at Rf= 0.43. The mixture was quenched with saturated NH_4Cl (10.0 ml), extracted with ethyl acetate (3*30 mL), washed with brine and dried ($MgSO_4$). The solvent was stripped

off in vacuo to afford crude product which was purified by flash column chromatography on a silica gel using 15 % EtOAC/hexane to afford 0.61 g (44 % yield) of desired product as yellow oil. Mass spectrum (CI-NH_3): m/z 411.2 (M^+). The acetal was dissolved in acetone (15.0 mL) and treated with 3.0 M aqeous HCl (30.0 mL) at room temperature. The reaction mixture was stirred for 24 h at this temperature and TLC (30:70 EtOAc/hexane) showed a new spot at Rf=0.55. It was then quenched with saturated NaCl (50.0 ml), extracted with ethyl acetate (3*50 mL), washed with brine and dried ($MgSO_4$). The solvent was removed in vacuum to afford yellow liquid and purified the crude by flash column chromatography on a silica gel using 15 % EtOAC/hexane to afford 0.28 g (51 % yield) of desired product as yellow solid (mp 85-86 °C). ^1H NMR ($CDCl_3$): ∂ 0.785 (m, 6H, 2*CH_3), 1.28-1.33 (t, 3H, CH_3), 1.90-2.23 (m, 4H, 2*CH_2), 2.74-2.82 (q, 2H, CH_2), 3.98-4.05 (m, 1H, CH), 7.34-7.37 (d, 1H, aromatic), 7.45-7.46 (d, 1H, aromatic), 7.55-7.58 (d, 1H, aromatic). Mass spectrum (CI-NH_3): m/z 367 (M^+). Anal. calcd for $C_{18}H_{20}Cl_2N_2O_2$: C, 58.87; H, 5.50; N, 7.64. Found: C, 58.91; H, 5.60; N, 7.44.

Part F: 4-(2,4-dichlorophenyl)-2-ethyl-1-(1-ethyl)propyl-imidazo[4,5-d]pyridazine:

A mixture of part E material (0.110 g, 0.0003 moles) in ethanol (15 mL) was treated with anhydrous hydrazine (0.125 g, 0.0039 moles) and refluxed under nitrogen for 4h. TLC (1:10 MeOH/CH_2Cl_2) showed a new spot at Rf=0.6. The solvent was removed under vacuum and purified the crude by flash column chromatography on a silica gel using 1:100 MeOH/CH_2Cl_2 to afford 105 mg (97 % yield) of the product as yellow oil and tituration of the oil with diethyl ether (1.0 mL) gave 65 mg of white crystalline solid (mp 136-137 °C). ^1H NMR ($CDCl_3$): ∂ 0.82-0.87 (t, 6H, 2*CH_3), 1.41-1.46 (t, 3H, CH_3), 2.05-2.21 (m, 4H, 2*CH_2), 2.95-3.03 (q, 2H, CH_2), 4.16-4.26 (m, 1H, CH), 7.41-7.44 (d, 1H, aromatic), 7.58-7.59 (d, 1H, aromatic), 7.64-7.67 (d, 1H, aromatic), 9.49 (s, 1H, 9 CH). Mass spectrum (CI-NH_3): m/z 363 (M^+). Anal. calcd for

$C_{18}H_{20}Cl_2N_4$: C, 59.51; H, 5.56; N, 15.42. Found: C, 59.53; H, 5.79; N, 14.70.

Example 95

4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-c]pyridazine

Part A: 4-Ethoxycarbonyl-5-(2,4-dichlorophenyl)-1,6-dihydropyridazin-3-one:

A 1M solution of $TiCl_4$ in CH_2Cl_2 (100 mL) was slowly added via syringe to anhydrous THF (500 mL) cooled to -5°C under N_2 with vigorous stirring. After stirring for 15 min, a solution of 2,2',4'-trichloroacetophenone (11g, 49.2 mmol) in THF was added to the mixture, followed by addition of diethyl malonate (7.4 mL, 48.4 mmol). Pyridine (16.5 mL) was then added dropwise, and the reaction mixture was stirred for 16h at room temperature. The mixture was then partitioned between Et_2O and water, and the aqueous layer was washed with Et_2O. Organic extracts were combined and dried over $MgSO_4$, filtered and evaporated in vacuo to afford the olefin as a pale yellow oil.

To a solution of the olefin in EtOH was added 1.5 equivalents of hydrazine monohydrate and 1.5 equivalents of diisopropylethylamine. The mixture was refluxed for 4h, then evaporated in vacuo. The residue was chromatographed on silica gel (100% Hexane to 20% EtOAc/Hexane gradient) to yield 5.8 g of a pale yellow solid. ^1H NMR (300MHz, $CDCl_3$): ∂ 9.39 (s, 1H), 7.42-7.26 (m, 3H), 4.23 (quart., 2H), 3.6 (m, 1H), 3.33-3.11 (m, 2H), 1,27 (t, 3H).

Part B: 3-Bromo-4-ethoxycarbonyl-5-(2,4-dichlorophenyl)pyridazine:

To a solution of 1.1 g of product from Part A in toluene was added 2 equivalents of $POBr_3$ and the mixture was refluxed for 3h. The reaction mixture was evaporated in vacuo and the residue was chromatographed on silica gel to yield desired product (100% Hexane to 15% EtOAc/Hex gradient). Mass spectrum (APcI): $(M+H)^+$ m/z 374.8 (60%), 376.8 (100%), 378.8 (43%).

Part C: 4-Amino-3-bromo-5-(2,4-dichlorophenyl) pyridazine:

To a solution of product from Part B in THF was added a solution of 5 equivalents of LiOH monohydrate in water. A small amount of MeOH was added to make the mixture homogenous. The reaction mixture was stirred at room temperature for 3h. The mixture was then partitioned between Et_2O and 1N HCl. The organic extract was dried over $MgSO_4$, filtered, and evaporated in vacuo to give the acid.

To a solution of the acid in t-BuOH was added 1.1 equivalents of both DPPA (diphenyphosphorylazide) and triethyamine. The reaction mixture was refluxed for 16h, then concentrated in vacuo. The residue was partitioned between Et_2O and water. The organic extract was dried over $MgSO_4$, filtered, and evaporated in vacuo. This residue was dissolved in CH_2Cl_2 and trifluoroacetic acid was added. This solution was stirred at room temperature for 4h, then evaporated in vacuo to afford the crude amine.

Part D: 4-(2,4-Dichlorophenyl)-2-ethyl-1-(1-cyclopropyl)propyl-imidazo[4,5-c]pyridazine:

To a mixture of the amine in toluene is added 1-cyclopropyl-1-propylamine hydrochloride (1.2 equivalents), sodium *t*-butoxide (2.5 equivalents), $Pd_2(dba)_3$ (0.05 equivalents), and BINAP (0.025 equivalents). The reaction mixture is stirred at 70°C for 16h. The mixture is then cooled and partitioned between Et_2O and water. The organic extract is dried over $MgSO_4$, filtered, and evaporated in vacuo. To the crude residue is added triethylorthopropionate and 1 drop of conc. HCl and the mixture is refluxed for 3h then evaporated in vacuo. To this residue is added *o*-xylene and *p*-toluenesulfonic acid, and this mixture is refluxed for 3h then evaporated in vacuo. The residue is chromatographed on silica gel (100% hexane to 40% EtOAc/Hexane gradient) to yield the title compound.

Example 1121
Synthesis of 2-ethyl-1-(1-ethyl)propyl-4-(2,4,6-trimethylphenyl)-imidazo[4,5-d]pyridazine

Part A: 2-Ethyl-1-(1-ethyl)propyl-4-(2,4,6-trimethylbenzoyl)-1H-imidazole-5-carboxaldehyde: A mixture of Part D material of Example 1 (0.82 g, 0.0030 moles) in THF (20.0 mL) was cooled to - 78 °C and then added dropwise 1.6 M n-BuLi in hexane (2.0 mL, 0.0033moles) over 15 mins under nitrogen atmosphere. The mixture was stirred at -78 °C for 3 h and then added a solution of 2,4,6-trimethylbenzoyl chloride (0.60 g, 0.0033 moles) in THF (5.0 mL) over 15 mins. The mixture was stirred at -78 °C for 6 h followed by room temperature overnight for 16 h and TLC (30:70 EtOAc / hexane) showed both starting material and product had same Rf values. The mixture was quenched with saturated NH_4Cl (10.0 ml), extracted with ethyl acetate (3*30 mL), washed with brine and dried ($MgSO_4$). The solvent was stripped off in vacuo to afford crude product (1.0 g) as yellow semi solid. Mass spectrum (APcI-positive): m/z 385.4 (M+H). The acetal was dissolved in acetone (15.0 mL) and treated with 3.0 M aqeous HCl (30.0 mL) at room temperature. The reaction mixture was stirred for 24 h at this temperature and TLC (30:70 EtOAc / hexane) showed a new spot at Rf=0.55 along with unreacted starting material acetal. Therefore continued further for 24 h and found to contain still some unreacted starting material. It was then quenched with saturated NaCl (50.0 ml), extracted with ethyl acetate (3*50 mL), washed with brine and dried ($MgSO_4$). The solvent was removed in vacuum to afford yellow liquid and purified the crude by flash column chromatography on a silica gel using dichloromethane as eluent to afford 0.3 g (29 % yield) of desired product as yellow solid (mp 119-120 °C). ^1H NMR ($CDCl_3$): ? 0.779 (m, 6H, 2*CH_3), 1.26-1.31 (t, 3H, CH_3), 1.90-1.95 (m, 4H, 2*CH_2), 2.16-2.31 (2 S, 9H, aromatic CH_3), 2.74-2.81 (q, 2H, CH_2), 3.98-4.05 (m,

1H, CH), 6.87 (s, 2H, aromatic), 10.3 (s, 1H, CHO). Mass spectrum (CI-NH_3): m/z 341 (M+H). Anal. calcd for $C_{21}H_{28}N_2O_2$: C, 74.08; H, 8.30; N, 8.24. Found: C, 74.33; H, 8.41; N, 8.18.

Part B: Title Compound: A mixture of Part A material of Example 1121 (0.2 g, 0.00059 moles) in ethanol (15 mL) was treated with anhydrous hydrazine (0.245 g, 0.0077 moles) and refluxed under nitrogen for 1h. TLC (1:50 MeOH / CH_2Cl_2) showed a new spot at Rf=0.45. The solvent was removed under vacuum and purified the crude by treatment with ethanol to afford white solid (0.2 g, mp 164-165 °C). ^1H NMR ($CDCl_3$): ? 0.77-0.82 (t, 6H, 2*CH_3), 1.24-1.29 (t, 3H, CH_3), 1.86-1.92 (m, 4H, 2*CH_2), 2.14 (s, 6H, 2*CH_3), 2.29 (s, 3H, CH_3), 2.68-2.76 (q, 2H, CH_2), 5.52 (bs, 3H, CH&NH_2), 6.85 (s, 2H, aromatic), 8.16 (s, 1H,-CH=N). Mass spectrum (CI-NH_3): m/z 355 (M+H). The reaction stopped at hydrazone stage and failed to cyclize even after 48 h in refluxing ethanol. The hydrazone (0.16 g, 0.45 mmol) was taken in 10 mL of ethylene glycol and refluxed for 2h at 200 °C. Mass spectrum (CI-NH_3): m/z 337 (m+H) revealed desired product and cooled the reaction mixture to room temp. and diluted with 25 ml of water, extracted with ethyl acetate (3*15 mL), washed with brine and dried ($MgSO_4$). The crude was purified by flash column chromatography on a silica gel using 1: 50 MeOH / CH_2Cl_2 to afford 71 mg (47 % yield) of the product as yellow crystalline solid (mp 151-152 °C). ^1H NMR ($CDCl_3$): ? 0.82-0.87 (t, 6H, 2*CH_3), 1.35-1.41 (t, 3H, CH_3), 2.0 (s, 6H, 2*CH_3), 2.1-2.17 (q, 4H, CH_2), 2.37 (s, 3H, CH_3), 2.92-3.0 (q, 2H, CH_2), 4.16-4.22 (m, 1H, CH), 6.98 (s, 2H, aromatic), 9.46 (s, 1H, 9 CH). Mass spectrum (CI-NH_3): m/z 337 (M+H). Anal. calcd for $C_{21}H_{28}N_4$: C, 74.96; H, 8.40; N, 16.65. Found: C, 74.77; H, 8.62; N, 15.42.

Example 1122

4-(2,4-dichloro-5-fluorophenyl)-2-ethyl-1-(1-ethyl)propyl-imidazo[4,5-d]pyridazine

Part A: 2-ethyl-1-(1-ethyl)propyl-4-(2,4-dichloro-5-fluorobenzoyl)-1H-imidazole-5-carboxaldehyde : A mixture of Part D material of Example 1 (0.82 g, 0.0030 moles) in THF (20.0 mL) was cooled to - 78 °C and then added dropwise 1.6 M n-BuLi in hexane (2.0 mL, 0.0033moles) over 15 mins under nitrogen atmosphere. The mixture was stirred at -78 °C for 3 h and then added a solution of 2,4-dichloro-5-F-benzoyl chloride (0.75 g, 0.0033 moles) in THF (5.0 mL) over 15 mins. The mixture was stirred at -78 °C for 6 h followed by room temperature overnight for 16 h and TLC (30:70 EtOAc / hexane) showed absence of starting material (Rf=0.5) and a new spot for the product at Rf=0.64. The mixture was quenched with saturated NH_4Cl (25.0 ml), extracted with ethyl ether (3*30 mL), washed with brine and dried ($MgSO_4$). The solvent was stripped off in vacuo to afford crude product (1.5 g) as yellow oil and purified by flash column chromatography on a silica gel using dichloromethane as eluent to afford desired product as colorless viscous oil (0.62 g, 48 %). ^1H NMR ($CDCl_3$): ? 0.86-0.91 (t, 6H, 2*CH_3), 1.25-1.30 (t, 3H, CH_3), 1.83-1.92 (q, 4H, 2*CH_2), 2.70-2.75 (q, 2H, CH_2), 2.74-2.81 (q, 2H, CH_2), 4.04-4.18 (m, 4H, 2*OCH_2), 4.41-4.51 (m, 1H, CH), 6.69 (s, 1H, -CH), 7.38-7.31 (d, 1H, aromatic), 7.45-7.47 (d, 1H, aromatic). Mass spectrum (APcI-positive): m/z 429.2 (M^+). The acetal was dissolved in acetone (15.0 mL) and treated with 3.0 M aqeous HCl (30.0 mL) at room temperature. The reaction mixture was stirred for 24 h at this temperature and TLC (30:70 EtOAc / hexane) showed a new spot at Rf=0.67 along with disappearence of starting material acetal. It was then quenched with saturated NaCl (50.0 ml), extracted with ethyl acetate (3*50 mL), washed with brine and dried ($MgSO_4$). The solvent was removed in

vacuum to afford yellow liquid and purified the crude by flash column chromatography on a silica gel using dichloromethane as eluent to afford 0.43 g (80 % yield) of desired product as white solid (mp 70-71°C). ^{1}H NMR ($CDCl_3$): ? 0.79 (m, 6H, 2*CH_3), 1.28-1.33 (t, 3H, CH_3), 1.90-2.2 (m, 4H, 2*CH_2), 2.74-2.82 (q, 2H, CH_2), 3.98-4.05 (m, 1H, CH), 7.42-7.45 (d, 1H, aromatic), 7.50-7.52 (d, 1H, aromatic), 10.4 (s, 1H, CHO). Mass spectrum (CI-NH_3): m/z 385 (M^+). Anal. calcd for $C_{18}H_{19}N_2O_2Cl_2F_1$: C, 56.12; H, 4.97; N, 7.27. Found: C,56.27; H,4.95; N,7.12.

Part B: Title Compound: A mixture of Part A material of Example 1122 (0.230 g, 0.0006 moles) in ethanol (15 mL) was treated with anhydrous hydrazine (0.25 g, 0.0077 moles) and refluxed under nitrogen for 16 h. TLC (1:10 MeOH / CH_2Cl_2) showed a new spot at Rf=0.6. The solvent was removed under vacuum and purified the crude by flash column chromatography on a silica gel using 1:50 MeOH / CH_2Cl_2 to afford 194 mg of pale yellow oil and tituration of the oil with hexane (1.0 mL) gave 59 mg (26 %) of white crystalline solid (mp 85-87 °C). ^{1}H NMR ($CDCl_3$): ? 0.82-0.87 (t, 6H, 2*CH_3), 1.42-1.47 (t, 3H, CH_3), 2.08-2.21 (m, 4H, 2*CH_2), 2.98-3.03 (q, 2H, CH_2), 4.16-4.26 (m, 1H, CH), 7.53-7.56 (d, 1H, aromatic), 7.62-7.64 (d, 1H, aromatic), 9.50 (s, 1H, 9 CH). Mass spectrum (CI-NH_3): m/z 381 (M^+). HRMS calcd. for $C_{18}H_{20}Cl_2F_1N_4$: 381.1048. Found: 381.1057 (M+H).

Example 1123
2-Ethyl-1-(1-ethyl)propyl-4-(2,4-dimethoxybenzoyl)-1H-imidazole-5-carboxaldehyde

A mixture of Part D material of Example 1 (0.82 g, 0.0030 moles) in THF (20.0 mL) was cooled to - 78 °C and then added dropwise 1.6 M n-BuLi in hexane (2.0 mL, 0.0033moles) over 15 mins under nitrogen atmosphere. The mixture was stirred at -78 °C for 3 h and then added a

solution of 2,4 -dimethoxybenzoyl chloride (0.66 g, 0.0033 moles) in THF (5.0 mL) over 15 mins. The mixture was stirred at -78 °C for 6 h followed by room temperature overnight for 16 h and The mixture was stirred at -78 °C for 6 h followed by room temperature overnight for 16 h and TLC (30:70 EtOAc / hexane) showed absence of starting material (Rf=0.5) and a new spot for the product at Rf=0.57. The mixture was quenched with saturated NH_4Cl (25.0 ml), extracted with ethyl ether (3*30 mL), washed with brine and dried ($MgSO_4$). The solvent was stripped off in vacuo to afford crude product (1.3 g) as yellow oil and purified by flash column chromatography on a silica gel using 1:100 methanol / dichloromethane as eluent to afford desired product as pale yellow viscous oil (0.39 g, 32 %). Mass spectrum (APcI-positive): m/z 403.3 ($M+H^+$). The acetal was dissolved in acetone (15.0 mL) and treated with 3.0 M aqeous HCl (30.0 mL) at room temperature. The reaction mixture was stirred for 24 h at this temperature and TLC (1:10 $MeOH/CH_2Cl_2$) showed two new spots at Rf=0.92 & 0.62. It was then quenched with saturated NaCl (50.0 ml), extracted with ethyl acetate (3*50 mL), washed with brine and dried ($MgSO_4$). The solvent was removed in vacuum to afford yellow liquid and purified the crude by flash column chromatography on a silica gel using dichloromethane as eluent. to afford 0.17 g of desired product (Rf=0.62). Mass spectrum (CI-NH_3): m/z 359 (M+H). 7-13-98: The above aldehyde (0.17 g) was dissolved in ethanol (15.0 mL) and treated with hydrazine (0.25 mL). The mixture was refluxed overnight and TLC (1:10 $MeOH/CH_2Cl_2$) revealed a new spot at Rf=0.49. The solvent was stripped off in vacuum and purified the crude by flash column chromatography on a silica gel using (1:50 $MeOH/CH_2Cl_2$) as eluent to afford 84 mg colorless oil. The oil was crystallized from 1:10 hexane/ether to afford 64 mg of white solid (mp 126-127 °C). HRMS calcd for $C_{20}H_{27}N_4O_2$: 355.2133. Found: 355.2121 (M+H).

Example 1124

4-(2,4-dichlorophenyl)-2-ethyl-1-(1-ethyl)propyl-7-methylimidazo[4,5-d]pyridazine

Part A: 4-(2,4-dichlorobenzoyl)-2-ethyl-1-(1-ethyl)propyl-5-(1-hydroxyethyl)-1H-imidazole : A mixture of Part E material of Example 1 (0.587 g, 0.0016 moles) in THF (20 mL) was cooled to - 78 °C and then added dropwise 1.6 M MeLi in ether (1.0 mL, 0.0016 moles) over 5 mins. The mixture was stirred at -78 °C for 2 h and then quenched with water (5.0 ml) at -78 °C. The reaction mixture was extracted with ethyl ether (3*30 mL), washed with brine and stripped off the solvent in vacuum to afford yellow liquid. TLC (30:70 EtOAc/hexane) showed absence of starting material at Rf=0.69 and a new spot at Rf=0.4. Purified the crude by flash column chromatography on a silica gel using 10 % EtOAC/hexane to afford 0.470 g (77 % yield) of desired product as white solid (mp 125-126 °C). Mass spectrum (CI-NH_3): m/z=383 (M^+). Anal. calcd for $C_{19}H_{24}Cl_2N_2O_2$: C, 59.54; H, 6.31; N, 7.32. Found: C, 59.59; H, 6.28; N,7.16.

Part B: 5-Acetyl-4-(2,4-dichlorobenzoyl)-2-ethyl-1-(1-ethyl)propyl-1H-imidazole A solution of Part A material of Example 1124 (0.4 g, 0.00104 moles) in toluene(10 mL) was treated with MnO_2 (0.91 g, 0.0104 moles) and stirred at 75 °C for 40h. TLC (30:70 EtOAc/hexane) showed presence of starting material at Rf=0.4 and a new spot at Rf=0.57. Added additional MnO_2 (0.91 g) and continued for addtional 20 h at 75 °C. &-27-98: TLC revealed only trace amount of starting material and therefore cooled the reaction mixture to room temp and filtered through celite. The filterate was concentrated to afford 0.32 g of colorless oil and purified the crude by flash column chromatography on a silica gel using 15 % EtOAC/hexane to afford 0.258 g (65

% yield) of desired product as white solid (m.p. 63-64 °C). Mass spec (CI-NH_3): m/z=381 (M^+). Anal. calcd. for $C_{19}H_{22}Cl_2N_2O_2$: C, 59.85; H, 5.83; N, 7.36. Found: C, 59.97; H,5.80; N, 7.12.

Part C: Title Compound: imidazole A solution of Part B material of Example 1124 (0.130 g, 0.00034 moles) in ethanol (10 mL) was treated with anhydrous hydrazine (0.142 g, 0.0044 moles) and refluxed under nitrogen for 3h. TLC (1:10 MeOH / CH_2Cl_2) showed a new spot at Rf=0.55. The solvent was removed under vacuum and purified the crude by flash column chromatography on a silica gel using 50:50 EtOAc / hexane to afford 53 mg (41 % yield) of the product as white solid after tituration of the oil with diethyl ether (mp 128-129 °C). Mass spectrum (CI-NH_3): m/z 377 (M^+). Anal. calcd. for $C_{19}H_{22}Cl_2N_4$: C, 60.48; H, 5.89; N, 14.89. Found: C, 59.40; H, 5.72; N, 14.46.

Example 1125
4-(2,4-dichlorophenyl)-2-ethyl-1-(1-ethyl)propyl-7-propoxyimidazo[4,5-d]pyridazine

Part A: Methyl 4-(2,4-dichlorobenzoyl)-2-ethyl-1-(1-ethyl)propyl-1H-imidazole-5-carboxalate: A mixture of Part E material of Example 1 (0.367 g, 0.001 moles) in methanol (60 mL) was treated with NaCN (Aldrich, 0.245 g, 0.005 moles, 5 equi.), AcOH (Baker, 96 mg; 0.0016 moles, 1.6 equiv.) and MnO_2, activated (Aldich, 1.24 g; 0.021 moles, 21 equiv.). The resulting mixture was stirred at room temp under nitrogen for 18 h. TLC (1:50 MeOH/CH_2Cl_2) revealed absence of starting material at Rf=0.8 and showed a new spot at Rf=0.44. Mass spec. revealed desired product (m/z=397). The reaction mixture was filtered through celite, washed with methanol, concentrated in vacuo and the crude was purified by flash column chromatography on a silica gel using 1:100 MeOH/CH_2Cl_2 as eluent to afford

320 mg (mp 73-74 °C, 81 %) of white solid after crystallization from hexane. Anal. calcd. for $C_{19}H_{22}N_2O_3Cl_2$: C,57.44; H,5.58; N,7.05. Found: C,57.31; H,5.45; N,6.85.

Part B: 4-(2,4-dichlorophenyl)-2-ethyl-1-(1-ethyl)propyl-imidazo[4,5-d]pyridazin-7-one: A mixture of Part A material of example 1125 (0.100 g, 0.00025 moles) in ethanol (10 mL) was treated with anhydrous hydrazine (0.105 g, 0.0033 moles) and refluxed under nitrogen for 48 h. TLC (30:70 EtOAc/hexane) showed a new spot at Rf=0.35. The solvent was removed under vacuum and purified the crude by flash column chromatography on a silica gel using 15:50 EtOAc / hexane intially and then methanol to afford 70 mg (74 % yield) of the product as white solid after tituration of the oil with diethyl ether (mp 246-247 °C). Mass spectrum (CI-NH_3) m/z=379 (M^+).

Part C: Title Compound: A mixture of Part B material of example 1125 (0.1 g, 0.264 mmol) in benzene (5.0 mL) was treated with n-Bu_4NBr (8.5 mg, 0.0264 mmol), powdered KOH (15 mg, 0.264 mmol) and 1-iodopropane (0.134 g, 0.79 mmol). The mixture was stirred at room temp overnight and TLC (1:50 MeOH/CH_2Cl_2) showed two new spots at Rf=0.73 and Rf=0.46. The reaction mixture was diluted with EtOAc (10 mL), washed with brine (10 mL), dried with $MgSO_4$ and concentrated to a residue. The crude was purified by flash column chromatography on a silica gel using dichloromethane as eluent to afford 56 mg (51 % yield) of the N-propyl product as colorless oil. Mass spectrum (CI-NH_3): m/z=421. Further elution of the column with 1:50 MeOH/CH_2Cl_2 gave 11 mg (10 % yield) of oil which was crystallized from ether to afford 7-propoxy derivative as awhite solid (m.p. 120-121 °C). Mass spec. (CI-NH_3): m/z=421. HRMS calcd for $C_{21}H_{27}N_4OCl_2$: 421.1561. Found: 421.1569 (M+H).

Example 1126
7-chloro-4-(2,4-dichlorophenyl)-2-ethyl-1-(1-methyl)butyl-imidazo[4,5-d]pyridazine

Part A: 4,5-dibromo-2-ethyl-1-(1-methyl)butyl-1H-imidazole:

A mixture of part A material of example 1 (59 g g, 0.233 moles), triphenylphosphine (67.1 g, 0.256 moles) and molecular sieves (10 g) in THF (715 mL) was cooled to 0 to - 5 °C and then added 2-pentanol (34.79 g, 0.279 moles) under nitrogen atmosphere. The mixture was stirred at 0 °C for 30 mins and then added disopropylazodicarboxylate (50.33 g, 0.256 moles) dropwise over 20 mins. The mixture was stirred at 0 °C for 2h followed by room temperature for 2 days and TLC (1:50 MeOH / CH_2Cl_2) revealed a new spot at Rf=0.5. The undissolved material was filtered, washed with dichloromethane and stripped off the solvent in vacuum to afford yellow liquid. The crude was purified by flash column chromatography using chloroform as eluent to afford 41.5 g (55 %) of colorless oil. ^1H NMR ($CDCl_3$): ? 0.91 (t, 3H, 2*CH_3), 1.27 (m, 2H, CH_2), 1.31 (t, 3H, CH_3), 1.53 (d, 3H, CH_3), 1.78 (m, 1H), 2.04 (m, 1H), 2.71 (q, 2H) and 4.34 (m,1H). Mass spectrum (CI-NH_3): m/z 325.0 (M+H).

Part B: 4-bromo-2-ethyl-1-(1-methyl)butyl-1H-imidazole-5-carboxaldehyde :

A solution of imidazole (37.5 g, 0.116 mol) in THF (250 mL) was cooled to -78 °C and then added dropwise 1.6 M n-BuLi(76 mL, 0. 122 mol) in hexane over 45 mins. The mixture was stirred at -78 °C for 1h (brown solution) and then added DMF (27 g, 0.348 moles) dropwise over 30 mins. The mixture was stirred at -78 °C for 60 mins. The reaction mixture was quenched with satd. amm. chloride (100 mL) at -78 °C and brought to room temp. The reaction mixture was extracted with ethyl ether (3*100

mL), washed with brine and dried with anhyd. $MgSO_4$. The solvent was evaporated under reduced pressure to afford 31.6 g of crude yellow oil. The NMRof the crude revealed formation of 4-bromo-2-ethyl-1-(1-methyl)butyl-1H-imidazole along with desired product in the ratio of 3:7. The TLC of the undesired 4-bromo-2-ethyl-1-(1-methyl)butyl-1H-imidazole is visible under iodine exposure (Rf=0.45). The crude was purified by flash column chromatography on a silica gel using 1% MeOH to afford 18.5 g (59 % yield) of colorless oil. Mass spec : m/z=273. Anal. calcd. for $C_{11}H_{17}N_2OBr$; C, 48.36; H, 6.27, N, 10.25. Found): C, 48.64; H, 6.01; N, 10.00.

Part C: 4-bromo-2-ethyl-1-(1-methyl)butyl-1H-imidazole-5-carboxaldehyde ethylene acetal: A mixture of Part B material of example 1126 (18.5 g, 0.068 moles) in benzene (250 mL) was treated with ethylene glycol (16.4 g, 0.264 moles), pyridine (2.7 g, 0.034 moles) and p-toluenesulfonic acid monohydrate (6.5 g, 0.034 moles). The reaction mixture was heated at reflux in a 20 mL capacity Dean-Stark trap equipped apparatus for 36h. TLC (30:70 EtOAc/hexane) revealed a new spot at Rf=0.42 (visible under iodine) along with trace amount of starting material (Rf=0.54). The reaction mixture was cooled to room temperature, diluted with EtOAc (250 mL), washed with 10 % sodium bicarbonate (2*250 mL), brine and dried ($MgSO_4$). The solvent was evaporated under reduced pressure to furnish white solid (20.7 g, mp 69-70 °C, 96 %). The crude was very pure by NMR. Mass spectrum (CI-NH_3): m/z 317.1 (M^+). Anal. calcd. for $C_{13}H_{22}N_2O_2Br_1$; C, 49.22; H, 6.67, N, 8.83. Found: C, 49.38; H, 6.62; N, 8.68.

Part D: 4-(2,4-dichlorobenzoyl)-2-ethyl-1-(1-methyl)butyl-1H-imidazole-5-carboxaldehyde: A solution of Part C material of Example 1126 (2.3 g, 5.6 mmol) in acetone (60 mL) was cooled to 15 °C and then added 3M aq. HCl (120 mL) over

15 mins. The mixture was stirred below 30 °C for 24 h. TLC (30:70 EtOAc/hexane) showed a new spot at Rf=0.58 along with disappearence of starting material (Rf=0.43). The solvent was removed under vacuum, extracted with ethyl acetate (3*50 mL), washed with brine and stripped off the solvent in vacuum to afford yellow liquid (2.4 g). The crude was purified by flash column chromatography on a silica gel using dichloromethane as eluent to afford 1.46 g (71 % yield) of desired product as yellow solid (mp 43-44 °C). Anal. calcd for $C_{18}H_{20}Cl_2N_2O_2$: C, 58.87; H, 5.50; N, 7.64. Found: C, 58.96; H, 5.34; N, 7.46. Mass spec. (NH_3-CI): m/z=367

Part E: Methyl 4-(2,4-dichlorobenzoyl)-2-ethyl-1-(1-methyl)butyl-1H-imidazole-5-carboxalate: A mixture of Part D material of Example 1126 (1.0 g, 0.0027 moles) in methanol (50 mL) was treated with NaCN (Aldrich, 0.67 g, 0.0136 moles, 5 equi.), AcOH (Baker, 260 mg; 0.00432 moles, 1.6 equiv.) and MnO_2, activated (Aldrich, 3.34 g, 0.057 moles, 21 equiv.). The resulting mixture was stirred at room temp under nitrogen for 20 h. TLC (30:70 EtOAc/hexane) revealed absence of starting material at Rf=0.58 and showed a new spot at Rf=0.4. The reaction mixture was filtered through celite, washed with methanol, concentrated in vacuo. The residue was diluted with water, extracted with ethyl acetate, washed with brine, dried and concentrated in vacuo to afford 0.98 g of yellow oil. The crude was purified by flash column chromatography on a silica gel using 30:70 EtOAc/hexane as eluent to afford 910 mg (85 %) of yellow oil. Mass spectrum : m/z=397. Anal. calcd. for $C_{19}H_{22}N_2O_3Cl_2$: C, 57.44; H, 5.58; N, 7.05. Found: C, 57.25; H, 5.70; N, 6.80.

Part F: 4-(2,4-dichlorophenyl)-2-ethyl-1-(1-ethyl)propyl-imidazo[4,5-d]pyridazin-7-one: A mixture of Part E material of Example 1126 (0.460 g,

0.00115 moles) in ethylene glycol (5 mL) was treated with anhydrous hydrazine (0.48 g, 0.0151 moles) and refluxed under nitrogen for 4h. TLC (30:70 EtOAc/hexane) revealed a new spot (Rf=0.44) along with disappearence of starting material (Rf=0.4). The reaction mixture was cooled to room temp and poured over 25 mL of water, extracted with EtOAc (3*15 mL), washed with brine and dried. The solvent was removed under vacuo and purified the crude by flash column chromatography on a silica gel using 15 % EtOAc/hexane to afford colorless oil which was crystallized from hexane to afford 310 mg of white solid (71 %, mp 217-18 °C). Mass spec. (CI-NH_3): m/z=379. Anal. calcd. for $C_{18}H_{20}N_4Cl_2O$: C, 57.00; H, 5.33; N, 14.77. Found: C, 57.02; H, 5.35; N, 14.59.

Part G: Title Compound: A mixture of Part F material of Example 1126 (0.270 g, 0.0071moles) in $POCl_3$ (3.0 mL) was refluxed under nitrogen for 8 h. TLC (30:70 EtOAc/hexane) revealed a new spot (Rf=0.48) along with disappearence of starting material (Rf=0.44) Excess $POCl_3$ from the reaction mixture was removed under vacuo, quenched with ice (10 g), extracted with EtOAc (3*15 mL), washed with brine and dried. The solvent was removed under vacuo and purified the crude by flash column chromatography on a silica gel using 30 % EtOAc/hexane to afford 80 mg of white solid (28 %, mp 124-125 °C). HRMS calcd for $C_{18}H_{20}N_4Cl_3$: 397.0753. Found: 397.0749 (M+H).

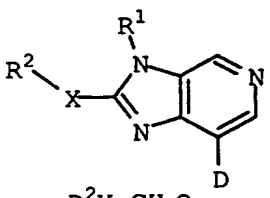
Example 1127

4-(2,4-dichlorophenyl)-2-ethyl-1-(1-methyl)butyl-7-methoxy-imidazo[4,5-d]pyridazine

A mixture of Part G material of Example 1126 (40 mg, 0.1 mmole) in MeOH (3.0 mL) was treated with 25 % NaOMe in MeOH (0.065 mL, 0.3 mmole) and refluxed under nitrogen for 6 h. TLC (30:70 EtOAc/hexane) revealed a new spot

(Rf=0.35) along with disappearence of starting material (Rf=0.48). The solvent from the reaction mixture was removed under vacuo, quenched with water (10 g), extracted with EtOAc (3*15 mL), washed with brine and dried. The solvent was removed under vacuo and purified the crude by recrystallizing from hexane to afford 36 mg of white solid (92 %, mp 119-120 °C). HRMS calcd for $C_{19}H_{23}N_4Cl_3O_1$: 393.1248. Found: 393.1246 (M+H).

Table 1



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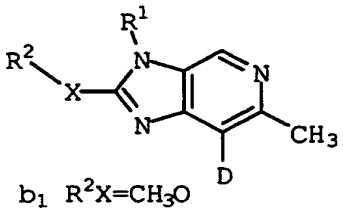
a_3 $R^2X=Me$
a_4 $R^2X=Et$
a_5 $R^2X=n\text{-}Pr$



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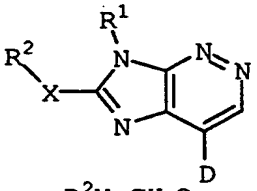
b_2 $R^2X=CH_3S$
b_3 $R^2X=Me$
b_4 $R^2X=Et$
b_5 $R^2X=n\text{-}Pr$



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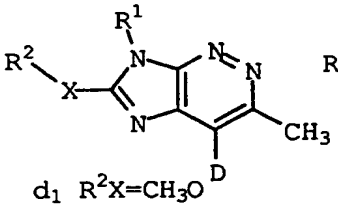
c_2 $R^2X=CH_3S$
c_3 $R^2X=Me$
c_4 $R^2X=Et$
c_5 $R^2X=n\text{-}Pr$



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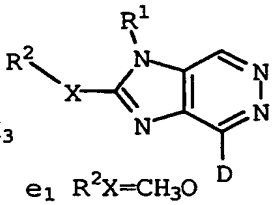
d_2 $R^2X=CH_3S$
d_3 $R^2X=Me$
d_4 $R^2X=Et$
d_5 $R^2X=n\text{-}Pr$



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e_2 $R^2X=CH_3S$
e_3 $R^2X=Me$
e_4 $R^2X=Et$
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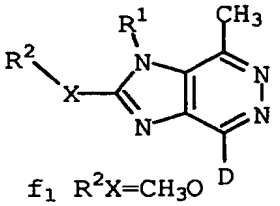

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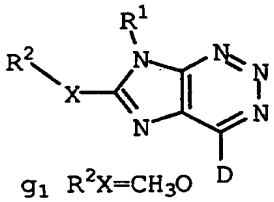
f_2 $R^2X=CH_3S$
f_3 $R^2X=Me$
f_4 $R^2X=Et$
f_5 $R^2X=n\text{-}Pr$



g_1 $R^2X=CH_3O$
g_2 $R^2X=CH_3S$
g_3 $R^2X=Me$
g_4 $R^2X=Et$
g_5 $R^2X=n\text{-}Pr$

Ex. #	R^1	D
1a	(cPr)$_2$CH	phenyl
2	phenyl(cPr)CH	phenyl
3	2-furanyl(cPr)CH	phenyl
4	3-furan(cPr)CH	phenyl

5	2-thienyl(cPr)CH	phenyl
6	3-thienyl(cPr)CH	phenyl
7	2-isoxazolyl(cPr)CH	phenyl
8	2-(5-CH_3-furanyl)(cPr)CH	phenyl
9	2-(4-CH_3-isoxazolyl)(cPr)CH	phenyl
10	cPr-CH(CH_3)	phenyl
11	1-cPr-CH(CH_2CH_3)	phenyl
12	1-cPr-CH($CH_2CH_2CH_3$)	phenyl
13	1-cPr-CH(CH_2OCH_3)	phenyl
14	1-cPr-CH($CH_2CH_2OCH_3$)	phenyl
15	(cBu)$_2$CH	phenyl
16	phenyl(cBu)CH	phenyl
17	2-furanyl(cBu)CH	phenyl
18	3-furan(cBu)CH	phenyl
19	2-thienyl(cBu)CH	phenyl
20	3-thienyl(cBu)CH	phenyl
21	2-isoxazolyl(cBu)CH	phenyl
22	2-(5-CH_3-furanyl)(cBu)CH	phenyl
23	2-(4-CH_3-isoxazolyl)(cBu)CH	phenyl
24	cBu-CH(CH_3)	phenyl
25	1-cBu-CH(CH_2CH_3)	phenyl
26	1-cBu-CH($CH_2CH_2CH_3$)	phenyl
27	1-cBu-CH(CH_2OCH_3)	phenyl
28	1-cBu-CH($CH_2CH_2OCH_3$)	phenyl
29	(cPr)$_2$CH	2-C1-4-MeO-phenyl
30	phenyl(cPr)CH	2-C1-4-MeO-phenyl
31	2-furanyl(cPr)CH	2-C1-4-MeO-phenyl
32	3-furan(cPr)CH	2-C1-4-MeO-phenyl
33	2-thienyl(cPr)CH	2-C1-4-MeO-phenyl
34	3-thienyl(cPr)CH	2-C1-4-MeO-phenyl
35	2-isoxazolyl(cPr)CH	2-C1-4-MeO-phenyl
36	2-(5-CH_3-furanyl)(cPr)CH	2-C1-4-MeO-phenyl
37	2-(4-CH_3-isoxazolyl)(cPr)CH	2-C1-4-MeO-phenyl
38	cPr-CH(CH_3)	2-C1-4-MeO-phenyl
39	1-cPr-CH(CH_2CH_3)	2-C1-4-MeO-phenyl
40	1-cPr-CH($CH_2CH_2CH_3$)	2-C1-4-MeO-phenyl
41	1-cPr-CH(CH_2OCH_3)	2-C1-4-MeO-phenyl
42	1-cPr-CH($CH_2CH_2OCH_3$)	2-C1-4-MeO-phenyl

	43	$(cBu)_2CH$	2-C1-4-MeO-phenyl
	44	phenyl(cBu)CH	2-C1-4-MeO-phenyl
	45	2-furanyl(cBu)CH	2-C1-4-MeO-phenyl
	46	3-furan(cBu)CH	2-C1-4-MeO-phenyl
5	47	2-thienyl(cBu)CH	2-C1-4-MeO-phenyl
	48	3-thienyl(cBu)CH	2-C1-4-MeO-phenyl
	49	2-isoxazolyl(cBu)CH	2-C1-4-MeO-phenyl
	50	2-(5-CH_3-furanyl)(cBu)CH	2-C1-4-MeO-phenyl
	51	2-(4-CH_3-isoxazolyl)(cBu)CH	2-C1-4-MeO-phenyl
10	52	cBu-CH(CH_3)	2-C1-4-MeO-phenyl
	53	1-cBu-CH(CH_2CH_3)	2-C1-4-MeO-phenyl
	54	1-cBu-CH($CH_2CH_2CH_3$)	2-C1-4-MeO-phenyl
	55	1-cBu-CH(CH_2OCH_3)	2-C1-4-MeO-phenyl
	56	1-cBu-CH($CH_2CH_2OCH_3$)	2-C1-4-MeO-phenyl
15	57	$(cPr)_2CH$	2-C1-4-CF_3-phenyl
	58	phenyl(cPr)CH	2-C1-4-CF_3-phenyl
	59	2-furanyl(cPr)CH	2-C1-4-CF_3-phenyl
	60	3-furan(cPr)CH	2-C1-4-CF_3-phenyl
	61	2-thienyl(cPr)CH	2-C1-4-CF_3-phenyl
20	62	3-thienyl(cPr)CH	2-C1-4-CF_3-phenyl
	63	2-isoxazolyl(cPr)CH	2-C1-4-CF_3-phenyl
	64	2-(5-CH_3-furanyl)(cPr)CH	2-C1-4-CF_3-phenyl
	65	2-(4-CH_3-isoxazolyl)(cPr)CH	2-C1-4-CF_3-phenyl
	66	cPr-CH(CH_3)	2-C1-4-CF_3-phenyl
25	67	1-cPr-CH(CH_2CH_3)	2-C1-4-CF_3-phenyl
	68	1-cPr-CH($CH_2CH_2CH_3$)	2-C1-4-CF_3-phenyl
	69	1-cPr-CH(CH_2OCH_3)	2-C1-4-CF_3-phenyl
	70	1-cPr-CH($CH_2CH_2OCH_3$)	2-C1-4-CF_3-phenyl
	71	$(cBu)_2CH$	2-C1-4-CF_3-phenyl
30	72	phenyl(cBu)CH	2-C1-4-CF_3-phenyl
	73	2-furanyl(cBu)CH	2-C1-4-CF_3-phenyl
	74	3-furan(cBu)CH	2-C1-4-CF_3-phenyl
	75	2-thienyl(cBu)CH	2-C1-4-CF_3-phenyl
	76	3-thienyl(cBu)CH	2-C1-4-CF_3-phenyl
35	77	2-isoxazolyl(cBu)CH	2-C1-4-CF_3-phenyl
	78	2-(5-CH_3-furanyl)(cBu)CH	2-C1-4-CF_3-phenyl
	79	2-(4-CH_3-isoxazolyl)(cBu)CH	2-C1-4-CF_3-phenyl
	80	cBu-CH(CH_3)	2-C1-4-CF_3-phenyl

	81	1-cBu-CH(CH_2CH_3)	2-Cl-4-CF_3-phenyl
	82	1-cBu-CH($CH_2CH_2CH_3$)	2-Cl-4-CF_3-phenyl
	83	1-cBu-CH(CH_2OCH_3)	2-Cl-4-CF_3-phenyl
	84	1-cBu-CH($CH_2CH_2OCH_3$)	2-Cl-4-CF_3-phenyl
5	85	(cPr)$_2$CH	2,4-diCl-phenyl
	86	phenyl(cPr)CH	2,4-diCl-phenyl
	87	2-furanyl(cPr)CH	2,4-diCl-phenyl
	88	3-furan(cPr)CH	2,4-diCl-phenyl
	89	2-thienyl(cPr)CH	2,4-diCl-phenyl
10	90	3-thienyl(cPr)CH	2,4-diCl-phenyl
	91	2-isoxazolyl(cPr)CH	2,4-diCl-phenyl
	92	2-(5-CH_3-furanyl)(cPr)CH	2,4-diCl-phenyl
	93	2-(4-CH_3-isoxazolyl)(cPr)CH	2,4-diCl-phenyl
	94	cPr-CH(CH_3)	2,4-diCl-phenyl
15	95	1-cPr-CH(CH_2CH_3)	2,4-diCl-phenyl
	96	1-cPr-CH($CH_2CH_2CH_3$)	2,4-diCl-phenyl
	97	1-cPr-CH(CH_2OCH_3)	2,4-diCl-phenyl
	98	1-cPr-CH($CH_2CH_2OCH_3$)	2,4-diCl-phenyl
	99	(cBu)$_2$CH	2,4-diCl-phenyl
20	100	phenyl(cBu)CH	2,4-diCl-phenyl
	101	2-furanyl(cBu)CH	2,4-diCl-phenyl
	102	3-furan(cBu)CH	2,4-diCl-phenyl
	103	2-thienyl(cBu)CH	2,4-diCl-phenyl
	104	3-thienyl(cBu)CH	2,4-diCl-phenyl
25	105	2-isoxazolyl(cBu)CH	2,4-diCl-phenyl
	106	2-(5-CH_3-furanyl)(cBu)CH	2,4-diCl-phenyl
	107	2-(4-CH_3-isoxazolyl)(cBu)CH	2,4-diCl-phenyl
	108	cBu-CH(CH_3)	2,4-diCl-phenyl
	109	1-cBu-CH(CH_2CH_3)	2,4-diCl-phenyl
30	110	1-cBu-CH($CH_2CH_2CH_3$)	2,4-diCl-phenyl
	111	1-cBu-CH(CH_2OCH_3)	2,4-diCl-phenyl
	112	1-cBu-CH($CH_2CH_2OCH_3$)	2,4-diCl-phenyl
	113	(cPr)$_2$CH	2,5-diCl-phenyl
	114	phenyl(cPr)CH	2,5-diCl-phenyl
35	115	2-furanyl(cPr)CH	2,5-diCl-phenyl
	116	3-furan(cPr)CH	2,5-diCl-phenyl
	117	2-thienyl(cPr)CH	2,5-diCl-phenyl
	118	3-thienyl(cPr)CH	2,5-diCl-phenyl

119	2-isoxazolyl(cPr)CH	2,5-diCl-phenyl
120	2-(5-CH_3-furanyl)(cPr)CH	2,5-diCl-phenyl
121	2-(4-CH_3-isoxazolyl)(cPr)CH	2,5-diCl-phenyl
122	cPr-$CH(CH_3)$	2,5-diCl-phenyl
123	1-cPr-$CH(CH_2CH_3)$	2,5-diCl-phenyl
124	1-cPr-$CH(CH_2CH_2CH_3)$	2,5-diCl-phenyl
125	1-cPr-$CH(CH_2OCH_3)$	2,5-diCl-phenyl
126	1-cPr-$CH(CH_2CH_2OCH_3)$	2,5-diCl-phenyl
127	$(cBu)_2CH$	2,5-diCl-phenyl
128	phenyl(cBu)CH	2,5-diCl-phenyl
129	2-furanyl(cBu)CH	2,5-diCl-phenyl
130	3-furan(cBu)CH	2,5-diCl-phenyl
131	2-thienyl(cBu)CH	2,5-diCl-phenyl
132	3-thienyl(cBu)CH	2,5-diCl-phenyl
133	2-isoxazolyl(cBu)CH	2,5-diCl-phenyl
134	2-(5-CH_3-furanyl)(cBu)CH	2,5-diCl-phenyl
135	2-(4-CH_3-isoxazolyl)(cBu)CH	2,5-diCl-phenyl
136	cBu-$CH(CH_3)$	2,5-diCl-phenyl
137	1-cBu-$CH(CH_2CH_3)$	2,5-diCl-phenyl
138	1-cBu-$CH(CH_2CH_2CH_3)$	2,5-diCl-phenyl
139	1-cBu-$CH(CH_2OCH_3)$	2,5-diCl-phenyl
140	1-cBu-$CH(CH_2CH_2OCH_3)$	2,5-diCl-phenyl
141	$(cPr)_2CH$	2-Cl-4-CF_3O-phenyl
142	phenyl(cPr)CH	2-Cl-4-CF_3O-phenyl
143	2-furanyl(cPr)CH	2-Cl-4-CF_3O-phenyl
144	3-furan(cPr)CH	2-Cl-4-CF_3O-phenyl
145	2-thienyl(cPr)CH	2-Cl-4-CF_3O-phenyl
146	3-thienyl(cPr)CH	2-Cl-4-CF_3O-phenyl
147	2-isoxazolyl(cPr)CH	2-Cl-4-CF_3O-phenyl
148	2-(5-CH_3-furanyl)(cPr)CH	2-Cl-4-CF_3O-phenyl
149	2-(4-CH_3-isoxazolyl)(cPr)CH	2-Cl-4-CF_3O-phenyl
150	cPr-$CH(CH_3)$	2-Cl-4-CF_3O-phenyl
151	1-cPr-$CH(CH_2CH_3)$	2-Cl-4-CF_3O-phenyl
152	1-cPr-$CH(CH_2CH_2CH_3)$	2-Cl-4-CF_3O-phenyl
153	1-cPr-$CH(CH_2OCH_3)$	2-Cl-4-CF_3O-phenyl
154	1-cPr-$CH(CH_2CH_2OCH_3)$	2-Cl-4-CF_3O-phenyl
155	$(cBu)_2CH$	2-Cl-4-CF_3O-phenyl
156	phenyl(cBu)CH	2-Cl-4-CF_3O-phenyl

	157	2-furanyl(cBu)CH	2-Cl-4-CF_3O-phenyl
	158	3-furan(cBu)CH	2-Cl-4-CF_3O-phenyl
	159	2-thienyl(cBu)CH	2-Cl-4-CF_3O-phenyl
	160	3-thienyl(cBu)CH	2-Cl-4-CF_3O-phenyl
5	161	2-isoxazolyl(cBu)CH	2-Cl-4-CF_3O-phenyl
	162	2-(5-CH_3-furanyl)(cBu)CH	2-Cl-4-CF_3O-phenyl
	163	2-(4-CH_3-isoxazolyl)(cBu)CH	2-Cl-4-CF_3O-phenyl
	164	cBu-CH(CH_3)	2-Cl-4-CF_3O-phenyl
	165	1-cBu-CH(CH_2CH_3)	2-Cl-4-CF_3O-phenyl
10	166	1-cBu-CH($CH_2CH_2CH_3$)	2-Cl-4-CF_3O-phenyl
	167	1-cBu-CH(CH_2OCH_3)	2-Cl-4-CF_3O-phenyl
	168	1-cBu-CH($CH_2CH_2OCH_3$)	2-Cl-4-CF_3O-phenyl
	169	(cPr)$_2$CH	2-Cl-4-CH_3-phenyl
	170	phenyl(cPr)CH	2-Cl-4-CH_3-phenyl
15	171	2-furanyl(cPr)CH	2-Cl-4-CH_3-phenyl
	172	3-furan(cPr)CH	2-Cl-4-CH_3-phenyl
	173	2-thienyl(cPr)CH	2-Cl-4-CH_3-phenyl
	174	3-thienyl(cPr)CH	2-Cl-4-CH_3-phenyl
	175	2-isoxazolyl(cPr)CH	2-Cl-4-CH_3-phenyl
20	176	2-(5-CH_3-furanyl)(cPr)CH	2-Cl-4-CH_3-phenyl
	177	2-(4-CH_3-isoxazolyl)(cPr)CH	2-Cl-4-CH_3-phenyl
	178	cPr-CH(CH_3)	2-Cl-4-CH_3-phenyl
	179	1-cPr-CH(CH_2CH_3)	2-Cl-4-CH_3-phenyl
	180	1-cPr-CH($CH_2CH_2CH_3$)	2-Cl-4-CH_3-phenyl
25	181	1-cPr-CH(CH_2OCH_3)	2-Cl-4-CH_3-phenyl
	182	1-cPr-CH($CH_2CH_2OCH_3$)	2-Cl-4-CH_3-phenyl
	183	(cBu)$_2$CH	2-Cl-4-CH_3-phenyl
	184	phenyl(cBu)CH	2-Cl-4-CH_3-phenyl
	185	2-furanyl(cBu)CH	2-Cl-4-CH_3-phenyl
30	186	3-furan(cBu)CH	2-Cl-4-CH_3-phenyl
	187	2-thienyl(cBu)CH	2-Cl-4-CH_3-phenyl
	188	3-thienyl(cBu)CH	2-Cl-4-CH_3-phenyl
	189	2-isoxazolyl(cBu)CH	2-Cl-4-CH_3-phenyl
	190	2-(5-CH_3-furanyl)(cBu)CH	2-Cl-4-CH_3-phenyl
35	191	2-(4-CH_3-isoxazolyl)(cBu)CH	2-Cl-4-CH_3-phenyl
	192	cBu-CH(CH_3)	2-Cl-4-CH_3-phenyl
	193	1-cBu-CH(CH_2CH_3)	2-Cl-4-CH_3-phenyl
	194	1-cBu-CH($CH_2CH_2CH_3$)	2-Cl-4-CH_3-phenyl

195	1-cBu-CH(CH_2OCH_3)	2-Cl-4-CH_3-phenyl
196	1-cBu-CH($CH_2CH_2OCH_3$)	2-Cl-4-CH_3-phenyl
197	(cPr)$_2$CH	2-Cl-4-CN-phenyl
198	phenyl(cPr)CH	2-Cl-4-CN-phenyl
199	2-furanyl(cPr)CH	2-Cl-4-CN-phenyl
200	3-furan(cPr)CH	2-Cl-4-CN-phenyl
201	2-thienyl(cPr)CH	2-Cl-4-CN-phenyl
202	3-thienyl(cPr)CH	2-Cl-4-CN-phenyl
203	2-isoxazolyl(cPr)CH	2-Cl-4-CN-phenyl
204	2-(5-CH_3-furanyl)(cPr)CH	2-Cl-4-CN-phenyl
205	2-(4-CH_3-isoxazolyl)(cPr)CH	2-Cl-4-CN-phenyl
206	cPr-CH(CH_3)	2-Cl-4-CN-phenyl
207	1-cPr-CH(CH_2CH_3)	2-Cl-4-CN-phenyl
208	1-cPr-CH($CH_2CH_2CH_3$)	2-Cl-4-CN-phenyl
209	1-cPr-CH(CH_2OCH_3)	2-Cl-4-CN-phenyl
210	1-cPr-CH($CH_2CH_2OCH_3$)	2-Cl-4-CN-phenyl
211	(cBu)$_2$CH	2-Cl-4-CN-phenyl
212	phenyl(cBu)CH	2-Cl-4-CN-phenyl
213	2-furanyl(cBu)CH	2-Cl-4-CN-phenyl
214	3-furan(cBu)CH	2-Cl-4-CN-phenyl
215	2-thienyl(cBu)CH	2-Cl-4-CN-phenyl
216	3-thienyl(cBu)CH	2-Cl-4-CN-phenyl
217	2-isoxazolyl(cBu)CH	2-Cl-4-CN-phenyl
218	2-(5-CH_3-furanyl)(cBu)CH	2-Cl-4-CN-phenyl
219	2-(4-CH_3-isoxazolyl)(cBu)CH	2-Cl-4-CN-phenyl
220	cBu-CH(CH_3)	2-Cl-4-CN-phenyl
221	1-cBu-CH(CH_2CH_3)	2-Cl-4-CN-phenyl
222	1-cBu-CH($CH_2CH_2CH_3$)	2-Cl-4-CN-phenyl
223	1-cBu-CH(CH_2OCH_3)	2-Cl-4-CN-phenyl
224	1-cBu-CH($CH_2CH_2OCH_3$)	2-Cl-4-CN-phenyl
225	(cPr)$_2$CH	2-CF_3-4-Cl-phenyl
226	phenyl(cPr)CH	2-CF_3-4-Cl-phenyl
227	2-furanyl(cPr)CH	2-CF_3-4-Cl-phenyl
228	3-furan(cPr)CH	2-CF_3-4-Cl-phenyl
229	2-thienyl(cPr)CH	2-CF_3-4-Cl-phenyl
230	3-thienyl(cPr)CH	2-CF_3-4-Cl-phenyl
231	2-isoxazolyl(cPr)CH	2-CF_3-4-Cl-phenyl
232	2-(5-CH_3-furanyl)(cPr)CH	2-CF_3-4-Cl-phenyl

233	2-(4-CH_3-isoxazolyl)(cPr)CH	2-CF_3-4-Cl-phenyl
234	cPr-CH(CH_3)	2-CF_3-4-Cl-phenyl
235	1-cPr-CH(CH_2CH_3)	2-CF_3-4-Cl-phenyl
236	1-cPr-CH($CH_2CH_2CH_3$)	2-CF_3-4-Cl-phenyl
237	1-cPr-CH(CH_2OCH_3)	2-CF_3-4-Cl-phenyl
238	1-cPr-CH($CH_2CH_2OCH_3$)	2-CF_3-4-Cl-phenyl
239	(cBu)$_2$CH	2-CF_3-4-Cl-phenyl
240	phenyl(cBu)CH	2-CF_3-4-Cl-phenyl
241	2-furanyl(cBu)CH	2-CF_3-4-Cl-phenyl
242	3-furan(cBu)CH	2-CF_3-4-Cl-phenyl
243	2-thienyl(cBu)CH	2-CF_3-4-Cl-phenyl
244	3-thienyl(cBu)CH	2-CF_3-4-Cl-phenyl
245	2-isoxazolyl(cBu)CH	2-CF_3-4-Cl-phenyl
246	2-(5-CH_3-furanyl)(cBu)CH	2-CF_3-4-Cl-phenyl
247	2-(4-CH_3-isoxazolyl)(cBu)CH	2-CF_3-4-Cl-phenyl
248	cBu-CH(CH_3)	2-CF_3-4-Cl-phenyl
249	1-cBu-CH(CH_2CH_3)	2-CF_3-4-Cl-phenyl
250	1-cBu-CH($CH_2CH_2CH_3$)	2-CF_3-4-Cl-phenyl
251	1-cBu-CH(CH_2OCH_3)	2-CF_3-4-Cl-phenyl
252	1-cBu-CH($CH_2CH_2OCH_3$)	2-CF_3-4-Cl-phenyl
253	(cPr)$_2$CH	2-CF_3-4-MeO-phenyl
254	phenyl(cPr)CH	2-CF_3-4-MeO-phenyl
255	2-furanyl(cPr)CH	2-CF_3-4-MeO-phenyl
256	3-furan(cPr)CH	2-CF_3-4-MeO-phenyl
257	2-thienyl(cPr)CH	2-CF_3-4-MeO-phenyl
258	3-thienyl(cPr)CH	2-CF_3-4-MeO-phenyl
259	2-isoxazolyl(cPr)CH	2-CF_3-4-MeO-phenyl
260	2-(5-CH_3-furanyl)(cPr)CH	2-CF_3-4-MeO-phenyl
261	2-(4-CH_3-isoxazolyl)(cPr)CH	2-CF_3-4-MeO-phenyl
262	cPr-CH(CH_3)	2-CF_3-4-MeO-phenyl
263	1-cPr-CH(CH_2CH_3)	2-CF_3-4-MeO-phenyl
264	1-cPr-CH($CH_2CH_2CH_3$)	2-CF_3-4-MeO-phenyl
265	1-cPr-CH(CH_2OCH_3)	2-CF_3-4-MeO-phenyl
266	1-cPr-CH($CH_2CH_2OCH_3$)	2-CF_3-4-MeO-phenyl
267	(cBu)$_2$CH	2-CF_3-4-MeO-phenyl
268	phenyl(cBu)CH	2-CF_3-4-MeO-phenyl
269	2-furanyl(cBu)CH	2-CF_3-4-MeO-phenyl
270	3-furan(cBu)CH	2-CF_3-4-MeO-phenyl

	271	2-thienyl(cBu)CH	2-CF_3-4-MeO-phenyl
	272	3-thienyl(cBu)CH	2-CF_3-4-MeO-phenyl
	273	2-isoxazolyl(cBu)CH	2-CF_3-4-MeO-phenyl
	274	2-(5-CH_3-furanyl)(cBu)CH	2-CF_3-4-MeO-phenyl
5	275	2-(4-CH_3-isoxazolyl)(cBu)CH	2-CF_3-4-MeO-phenyl
	276	cBu-CH(CH_3)	2-CF_3-4-MeO-phenyl
	277	1-cBu-CH(CH_2CH_3)	2-CF_3-4-MeO-phenyl
	278	1-cBu-CH($CH_2CH_2CH_3$)	2-CF_3-4-MeO-phenyl
	279	1-cBu-CH(CH_2OCH_3)	2-CF_3-4-MeO-phenyl
10	280	1-cBu-CH($CH_2CH_2OCH_3$)	2-CF_3-4-MeO-phenyl
	281	(cPr)$_2$CH	2-CF_3-4-n-PrO-phenyl
	282	phenyl(cPr)CH	2-CF_3-4-n-PrO-phenyl
	283	2-furanyl(cPr)CH	2-CF_3-4-n-PrO-phenyl
	284	3-furan(cPr)CH	2-CF_3-4-n-PrO-phenyl
15	285	2-thienyl(cPr)CH	2-CF_3-4-n-PrO-phenyl
	286	3-thienyl(cPr)CH	2-CF_3-4-n-PrO-phenyl
	287	2-isoxazolyl(cPr)CH	2-CF_3-4-n-PrO-phenyl
	288	2-(5-CH_3-furanyl)(cPr)CH	2-CF_3-4-n-PrO-phenyl
	289	2-(4-CH_3-isoxazolyl)(cPr)CH	2-CF_3-4-n-PrO-phenyl
20	290	cPr-CH(CH_3)	2-CF_3-4-n-PrO-phenyl
	291	1-cPr-CH(CH_2CH_3)	2-CF_3-4-n-PrO-phenyl
	292	1-cPr-CH($CH_2CH_2CH_3$)	2-CF_3-4-n-PrO-phenyl
	293	1-cPr-CH(CH_2OCH_3)	2-CF_3-4-n-PrO-phenyl
	294	1-cPr-CH($CH_2CH_2OCH_3$)	2-CF_3-4-n-PrO-phenyl
25	295	(cBu)$_2$CH	2-CF_3-4-n-PrO-phenyl
	296	phenyl(cBu)CH	2-CF_3-4-n-PrO-phenyl
	297	2-furanyl(cBu)CH	2-CF_3-4-n-PrO-phenyl
	298	3-furan(cBu)CH	2-CF_3-4-n-PrO-phenyl
	299	2-thienyl(cBu)CH	2-CF_3-4-n-PrO-phenyl
30	300	3-thienyl(cBu)CH	2-CF_3-4-n-PrO-phenyl
	301	2-isoxazolyl(cBu)CH	2-CF_3-4-n-PrO-phenyl
	302	2-(5-CH_3-furanyl)(cBu)CH	2-CF_3-4-n-PrO-phenyl
	303	2-(4-CH_3-isoxazolyl)(cBu)CH	2-CF_3-4-n-PrO-phenyl
	304	cBu-CH(CH_3)	2-CF_3-4-n-PrO-phenyl
35	305	1-cBu-CH(CH_2CH_3)	2-CF_3-4-n-PrO-phenyl
	306	1-cBu-CH($CH_2CH_2CH_3$)	2-CF_3-4-n-PrO-phenyl
	307	1-cBu-CH(CH_2OCH_3)	2-CF_3-4-n-PrO-phenyl
	308	1-cBu-CH($CH_2CH_2OCH_3$)	2-CF_3-4-n-PrO-phenyl

	309	$(cPr)_2CH$	2,4-diCF_3-phenyl
	310	phenyl(cPr)CH	2,4-diCF_3-phenyl
	311	2-furanyl(cPr)CH	2,4-diCF_3-phenyl
	312	3-furan(cPr)CH	2,4-diCF_3-phenyl
5	313	2-thienyl(cPr)CH	2,4-diCF_3-phenyl
	314	3-thienyl(cPr)CH	2,4-diCF_3-phenyl
	315	2-isoxazolyl(cPr)CH	2,4-diCF_3-phenyl
	316	2-(5-CH_3-furanyl)(cPr)CH	2,4-diCF_3-phenyl
	317	2-(4-CH_3-isoxazolyl)(cPr)CH	2,4-diCF_3-phenyl
10	318	cPr-CH(CH_3)	2,4-diCF_3-phenyl
	319	1-cPr-CH(CH_2CH_3)	2,4-diCF_3-phenyl
	320	1-cPr-CH($CH_2CH_2CH_3$)	2,4-diCF_3-phenyl
	321	1-cPr-CH(CH_2OCH_3)	2,4-diCF_3-phenyl
	322	1-cPr-CH($CH_2CH_2OCH_3$)	2,4-diCF_3-phenyl
15	323	$(cBu)_2CH$	2,4-diCF_3-phenyl
	324	phenyl(cBu)CH	2,4-diCF_3-phenyl
	325	2-furanyl(cBu)CH	2,4-diCF_3-phenyl
	326	3-furan(cBu)CH	2,4-diCF_3-phenyl
	327	2-thienyl(cBu)CH	2,4-diCF_3-phenyl
20	328	3-thienyl(cBu)CH	2,4-diCF_3-phenyl
	329	2-isoxazolyl(cBu)CH	2,4-diCF_3-phenyl
	330	2-(5-CH_3-furanyl)(cBu)CH	2,4-diCF_3-phenyl
	331	2-(4-CH_3-isoxazolyl)(cBu)CH	2,4-diCF_3-phenyl
	332	cBu-CH(CH_3)	2,4-diCF_3-phenyl
25	333	1-cBu-CH(CH_2CH_3)	2,4-diCF_3-phenyl
	334	1-cBu-CH($CH_2CH_2CH_3$)	2,4-diCF_3-phenyl
	335	1-cBu-CH(CH_2OCH_3)	2,4-diCF_3-phenyl
	336	1-cBu-CH($CH_2CH_2OCH_3$)	2,4-diCF_3-phenyl
	337	$(cPr)_2CH$	2-CF_3-4-F-phenyl
30	338	phenyl(cPr)CH	2-CF_3-4-F-phenyl
	339	2-furanyl(cPr)CH	2-CF_3-4-F-phenyl
	340	3-furan(cPr)CH	2-CF_3-4-F-phenyl
	341	2-thienyl(cPr)CH	2-CF_3-4-F-phenyl
	342	3-thienyl(cPr)CH	2-CF_3-4-F-phenyl
35	343	2-isoxazolyl(cPr)CH	2-CF_3-4-F-phenyl
	344	2-(5-CH_3-furanyl)(cPr)CH	2-CF_3-4-F-phenyl
	345	2-(4-CH_3-isoxazolyl)(cPr)CH	2-CF_3-4-F-phenyl
	346	cPr-CH(CH_3)	2-CF_3-4-F-phenyl

	347	1-cPr-CH(CH_2CH_3)	2-CF_3-4-F-phenyl
	348	1-cPr-CH($CH_2CH_2CH_3$)	2-CF_3-4-F-phenyl
	349	1-cPr-CH(CH_2OCH_3)	2-CF_3-4-F-phenyl
	350	1-cPr-CH($CH_2CH_2OCH_3$)	2-CF_3-4-F-phenyl
5	351	(cBu)$_2$CH	2-CF_3-4-F-phenyl
	352	phenyl(cBu)CH	2-CF_3-4-F-phenyl
	353	2-furanyl(cBu)CH	2-CF_3-4-F-phenyl
	354	3-furan(cBu)CH	2-CF_3-4-F-phenyl
	355	2-thienyl(cBu)CH	2-CF_3-4-F-phenyl
10	356	3-thienyl(cBu)CH	2-CF_3-4-F-phenyl
	357	2-isoxazolyl(cBu)CH	2-CF_3-4-F-phenyl
	358	2-(5-CH_3-furanyl)(cBu)CH	2-CF_3-4-F-phenyl
	359	2-(4-CH_3-isoxazolyl)(cBu)CH	2-CF_3-4-F-phenyl
	360	cBu-CH(CH_3)	2-CF_3-4-F-phenyl
15	361	1-cBu-CH(CH_2CH_3)	2-CF_3-4-F-phenyl
	362	1-cBu-CH($CH_2CH_2CH_3$)	2-CF_3-4-F-phenyl
	363	1-cBu-CH(CH_2OCH_3)	2-CF_3-4-F-phenyl
	364	1-cBu-CH($CH_2CH_2OCH_3$)	2-CF_3-4-F-phenyl
	365	(cPr)$_2$CH	2-CH_3-4-Cl-phenyl
20	366	phenyl(cPr)CH	2-CH_3-4-Cl-phenyl
	367	2-furanyl(cPr)CH	2-CH_3-4-Cl-phenyl
	368	3-furan(cPr)CH	2-CH_3-4-Cl-phenyl
	369	2-thienyl(cPr)CH	2-CH_3-4-Cl-phenyl
	370	3-thienyl(cPr)CH	2-CH_3-4-Cl-phenyl
25	371	2-isoxazolyl(cPr)CH	2-CH_3-4-Cl-phenyl
	372	2-(5-CH_3-furanyl)(cPr)CH	2-CH_3-4-Cl-phenyl
	373	2-(4-CH_3-isoxazolyl)(cPr)CH	2-CH_3-4-Cl-phenyl
	374	cPr-CH(CH_3)	2-CH_3-4-Cl-phenyl
	375	1-cPr-CH(CH_2CH_3)	2-CH_3-4-Cl-phenyl
30	376	1-cPr-CH($CH_2CH_2CH_3$)	2-CH_3-4-Cl-phenyl
	377	1-cPr-CH(CH_2OCH_3)	2-CH_3-4-Cl-phenyl
	378	1-cPr-CH($CH_2CH_2OCH_3$)	2-CH_3-4-Cl-phenyl
	379	(cBu)$_2$CH	2-CH_3-4-Cl-phenyl
	380	phenyl(cBu)CH	2-CH_3-4-Cl-phenyl
35	381	2-furanyl(cBu)CH	2-CH_3-4-Cl-phenyl
	382	3-furan(cBu)CH	2-CH_3-4-Cl-phenyl
	383	2-thienyl(cBu)CH	2-CH_3-4-Cl-phenyl
	384	3-thienyl(cBu)CH	2-CH_3-4-Cl-phenyl

	385	2-isoxazolyl(cBu)CH	2-CH_3-4-Cl-phenyl
	386	2-(5-CH_3-furanyl)(cBu)CH	2-CH_3-4-Cl-phenyl
	387	2-(4-CH_3-isoxazolyl)(cBu)CH	2-CH_3-4-Cl-phenyl
	388	cBu-CH(CH_3)	2-CH_3-4-Cl-phenyl
5	389	1-cBu-CH(CH_2CH_3)	2-CH_3-4-Cl-phenyl
	390	1-cBu-CH($CH_2CH_2CH_3$)	2-CH_3-4-Cl-phenyl
	391	1-cBu-CH(CH_2OCH_3)	2-CH_3-4-Cl-phenyl
	392	1-cBu-CH($CH_2CH_2OCH_3$)	2-CH_3-4-Cl-phenyl
	393	(cPr)$_2$CH	2-CH_3-4-MeO-phenyl
10	394	phenyl(cPr)CH	2-CH_3-4-MeO-phenyl
	395	2-furanyl(cPr)CH	2-CH_3-4-MeO-phenyl
	396	3-furan(cPr)CH	2-CH_3-4-MeO-phenyl
	397	2-thienyl(cPr)CH	2-CH_3-4-MeO-phenyl
	398	3-thienyl(cPr)CH	2-CH_3-4-MeO-phenyl
15	399	2-isoxazolyl(cPr)CH	2-CH_3-4-MeO-phenyl
	400	2-(5-CH_3-furanyl)(cPr)CH	2-CH_3-4-MeO-phenyl
	401	2-(4-CH_3-isoxazolyl)(cPr)CH	2-CH_3-4-MeO-phenyl
	402	cPr-CH(CH_3)	2-CH_3-4-MeO-phenyl
	403	1-cPr-CH(CH_2CH_3)	2-CH_3-4-MeO-phenyl
20	404	1-cPr-CH($CH_2CH_2CH_3$)	2-CH_3-4-MeO-phenyl
	405	1-cPr-CH(CH_2OCH_3)	2-CH_3-4-MeO-phenyl
	406	1-cPr-CH($CH_2CH_2OCH_3$)	2-CH_3-4-MeO-phenyl
	407	(cBu)$_2$CH	2-CH_3-4-MeO-phenyl
	408	phenyl(cBu)CH	2-CH_3-4-MeO-phenyl
25	409	2-furanyl(cBu)CH	2-CH_3-4-MeO-phenyl
	410	3-furan(cBu)CH	2-CH_3-4-MeO-phenyl
	411	2-thienyl(cBu)CH	2-CH_3-4-MeO-phenyl
	412	3-thienyl(cBu)CH	2-CH_3-4-MeO-phenyl
	413	2-isoxazolyl(cBu)CH	2-CH_3-4-MeO-phenyl
30	414	2-(5-CH_3-furanyl)(cBu)CH	2-CH_3-4-MeO-phenyl
	415	2-(4-CH_3-isoxazolyl)(cBu)CH	2-CH_3-4-MeO-phenyl
	416	cBu-CH(CH_3)	2-CH_3-4-MeO-phenyl
	417	1-cBu-CH(CH_2CH_3)	2-CH_3-4-MeO-phenyl
	418	1-cBu-CH($CH_2CH_2CH_3$)	2-CH_3-4-MeO-phenyl
35	419	1-cBu-CH(CH_2OCH_3)	2-CH_3-4-MeO-phenyl
	420	1-cBu-CH($CH_2CH_2OCH_3$)	2-CH_3-4-MeO-phenyl
	421	(cPr)$_2$CH	2,4-diCH_3-phenyl
	422	phenyl(cPr)CH	2,4-diCH_3-phenyl

423	2-furanyl(cPr)CH	2,4-diCH3-phenyl
424	3-furan(cPr)CH	2,4-diCH3-phenyl
425	2-thienyl(cPr)CH	2,4-diCH3-phenyl
426	3-thienyl(cPr)CH	2,4-diCH3-phenyl
427	2-isoxazolyl(cPr)CH	2,4-diCH3-phenyl
428	2-(5-CH3-furanyl)(cPr)CH	2,4-diCH3-phenyl
429	2-(4-CH3-isoxazolyl)(cPr)CH	2,4-diCH3-phenyl
430	cPr-CH(CH3)	2,4-diCH3-phenyl
431	1-cPr-CH(CH2CH3)	2,4-diCH3-phenyl
432	1-cPr-CH(CH2CH2CH3)	2,4-diCH3-phenyl
433	1-cPr-CH(CH2OCH3)	2,4-diCH3-phenyl
434	1-cPr-CH(CH2CH2OCH3)	2,4-diCH3-phenyl
435	(cBu)2CH	2,4-diCH3-phenyl
436	phenyl(cBu)CH	2,4-diCH3-phenyl
437	2-furanyl(cBu)CH	2,4-diCH3-phenyl
438	3-furan(cBu)CH	2,4-diCH3-phenyl
439	2-thienyl(cBu)CH	2,4-diCH3-phenyl
440	3-thienyl(cBu)CH	2,4-diCH3-phenyl
441	2-isoxazolyl(cBu)CH	2,4-diCH3-phenyl
442	2-(5-CH3-furanyl)(cBu)CH	2,4-diCH3-phenyl
443	2-(4-CH3-isoxazolyl)(cBu)CH	2,4-diCH3-phenyl
444	cBu-CH(CH3)	2,4-diCH3-phenyl
445	1-cBu-CH(CH2CH3)	2,4-diCH3-phenyl
446	1-cBu-CH(CH2CH2CH3)	2,4-diCH3-phenyl
447	1-cBu-CH(CH2OCH3)	2,4-diCH3-phenyl
448	1-cBu-CH(CH2CH2OCH3)	2,4-diCH3-phenyl
449	(cPr)2CH	2-CH3-4-(CH3)2N-phenyl
450	phenyl(cPr)CH	2-CH3-4-(CH3)2N-phenyl
451	2-furanyl(cPr)CH	2-CH3-4-(CH3)2N-phenyl
452	3-furan(cPr)CH	2-CH3-4-(CH3)2N-phenyl
453	2-thienyl(cPr)CH	2-CH3-4-(CH3)2N-phenyl
454	3-thienyl(cPr)CH	2-CH3-4-(CH3)2N-phenyl
455	2-isoxazolyl(cPr)CH	2-CH3-4-(CH3)2N-phenyl
456	2-(5-CH3-furanyl)(cPr)CH	2-CH3-4-(CH3)2N-phenyl
457	2-(4-CH3-isoxazolyl)(cPr)CH	2-CH3-4-(CH3)2N-phenyl
458	cPr-CH(CH3)	2-CH3-4-(CH3)2N-phenyl
459	1-cPr-CH(CH2CH3)	2-CH3-4-(CH3)2N-phenyl
460	1-cPr-CH(CH2CH2CH3)	2-CH3-4-(CH3)2N-phenyl

461	1-cPr-CH(CH_2OCH_3)	2-CH_3-4-$(CH_3)_2N$-phenyl
462	1-cPr-CH($CH_2CH_2OCH_3$)	2-CH_3-4-$(CH_3)_2N$-phenyl
463	$(cBu)_2CH$	2-CH_3-4-$(CH_3)_2N$-phenyl
464	phenyl(cBu)CH	2-CH_3-4-$(CH_3)_2N$-phenyl
465	2-furanyl(cBu)CH	2-CH_3-4-$(CH_3)_2N$-phenyl
466	3-furan(cBu)CH	2-CH_3-4-$(CH_3)_2N$-phenyl
467	2-thienyl(cBu)CH	2-CH_3-4-$(CH_3)_2N$-phenyl
468	3-thienyl(cBu)CH	2-CH_3-4-$(CH_3)_2N$-phenyl
469	2-isoxazolyl(cBu)CH	2-CH_3-4-$(CH_3)_2N$-phenyl
470	2-(5-CH_3-furanyl)(cBu)CH	2-CH_3-4-$(CH_3)_2N$-phenyl
471	2-(4-CH_3-isoxazolyl)(cBu)CH	2-CH_3-4-$(CH_3)_2N$-phenyl
472	cBu-CH(CH_3)	2-CH_3-4-$(CH_3)_2N$-phenyl
473	1-cBu-CH(CH_2CH_3)	2-CH_3-4-$(CH_3)_2N$-phenyl
474	1-cBu-CH($CH_2CH_2CH_3$)	2-CH_3-4-$(CH_3)_2N$-phenyl
475	1-cBu-CH(CH_2OCH_3)	2-CH_3-4-$(CH_3)_2N$-phenyl
476	1-cBu-CH($CH_2CH_2OCH_3$)	2-CH_3-4-$(CH_3)_2N$-phenyl
477	$(cPr)_2CH$	2-MeO-4-CH_3-phenyl
478	phenyl(cPr)CH	2-MeO-4-CH_3-phenyl
479	2-furanyl(cPr)CH	2-MeO-4-CH_3-phenyl
480	3-furan(cPr)CH	2-MeO-4-CH_3-phenyl
481	2-thienyl(cPr)CH	2-MeO-4-CH_3-phenyl
482	3-thienyl(cPr)CH	2-MeO-4-CH_3-phenyl
483	2-isoxazolyl(cPr)CH	2-MeO-4-CH_3-phenyl
484	2-(5-CH_3-furanyl)(cPr)CH	2-MeO-4-CH_3-phenyl
485	2-(4-CH_3-isoxazolyl)(cPr)CH	2-MeO-4-CH_3-phenyl
486	cPr-CH(CH_3)	2-MeO-4-CH_3-phenyl
487	1-cPr-CH(CH_2CH_3)	2-MeO-4-CH_3-phenyl
488	1-cPr-CH($CH_2CH_2CH_3$)	2-MeO-4-CH_3-phenyl
489	1-cPr-CH(CH_2OCH_3)	2-MeO-4-CH_3-phenyl
490	1-cPr-CH($CH_2CH_2OCH_3$)	2-MeO-4-CH_3-phenyl
491	$(cBu)_2CH$	2-MeO-4-CH_3-phenyl
492	phenyl(cBu)CH	2-MeO-4-CH_3-phenyl
493	2-furanyl(cBu)CH	2-MeO-4-CH_3-phenyl
494	3-furan(cBu)CH	2-MeO-4-CH_3-phenyl
495	2-thienyl(cBu)CH	2-MeO-4-CH_3-phenyl
496	3-thienyl(cBu)CH	2-MeO-4-CH_3-phenyl
497	2-isoxazolyl(cBu)CH	2-MeO-4-CH_3-phenyl
498	2-(5-CH_3-furanyl)(cBu)CH	2-MeO-4-CH_3-phenyl

499	2-(4-CH_3-isoxazolyl)(cBu)CH	2-MeO-4-CH_3-phenyl
500	cBu-CH(CH_3)	2-MeO-4-CH_3-phenyl
501	1-cBu-CH(CH_2CH_3)	2-MeO-4-CH_3-phenyl
502	1-cBu-CH($CH_2CH_2CH_3$)	2-MeO-4-CH_3-phenyl
503	1-cBu-CH(CH_2OCH_3)	2-MeO-4-CH_3-phenyl
504	1-cBu-CH($CH_2CH_2OCH_3$)	2-MeO-4-CH_3-phenyl
505	(cPr)$_2$CH	2-MeO-4-CF_3-phenyl
506	phenyl(cPr)CH	2-MeO-4-CF_3-phenyl
507	2-furanyl(cPr)CH	2-MeO-4-CF_3-phenyl
508	3-furan(cPr)CH	2-MeO-4-CF_3-phenyl
509	2-thienyl(cPr)CH	2-MeO-4-CF_3-phenyl
510	3-thienyl(cPr)CH	2-MeO-4-CF_3-phenyl
511	2-isoxazolyl(cPr)CH	2-MeO-4-CF_3-phenyl
512	2-(5-CH_3-furanyl)(cPr)CH	2-MeO-4-CF_3-phenyl
513	2-(4-CH_3-isoxazolyl)(cPr)CH	2-MeO-4-CF_3-phenyl
514	cPr-CH(CH_3)	2-MeO-4-CF_3-phenyl
515	1-cPr-CH(CH_2CH_3)	2-MeO-4-CF_3-phenyl
516	1-cPr-CH($CH_2CH_2CH_3$)	2-MeO-4-CF_3-phenyl
517	1-cPr-CH(CH_2OCH_3)	2-MeO-4-CF_3-phenyl
518	1-cPr-CH($CH_2CH_2OCH_3$)	2-MeO-4-CF_3-phenyl
519	(cBu)$_2$CH	2-MeO-4-CF_3-phenyl
520	phenyl(cBu)CH	2-MeO-4-CF_3-phenyl
521	2-furanyl(cBu)CH	2-MeO-4-CF_3-phenyl
522	3-furan(cBu)CH	2-MeO-4-CF_3-phenyl
523	2-thienyl(cBu)CH	2-MeO-4-CF_3-phenyl
524	3-thienyl(cBu)CH	2-MeO-4-CF_3-phenyl
525	2-isoxazolyl(cBu)CH	2-MeO-4-CF_3-phenyl
526	2-(5-CH_3-furanyl)(cBu)CH	2-MeO-4-CF_3-phenyl
527	2-(4-CH_3-isoxazolyl)(cBu)CH	2-MeO-4-CF_3-phenyl
528	cBu-CH(CH_3)	2-MeO-4-CF_3-phenyl
529	1-cBu-CH(CH_2CH_3)	2-MeO-4-CF_3-phenyl
530	1-cBu-CH($CH_2CH_2CH_3$)	2-MeO-4-CF_3-phenyl
531	1-cBu-CH(CH_2OCH_3)	2-MeO-4-CF_3-phenyl
532	1-cBu-CH($CH_2CH_2OCH_3$)	2-MeO-4-CF_3-phenyl
533	(cPr)$_2$CH	2-MeO-4-Cl-phenyl
534	phenyl(cPr)CH	2-MeO-4-Cl-phenyl
535	2-furanyl(cPr)CH	2-MeO-4-Cl-phenyl
536	3-furan(cPr)CH	2-MeO-4-Cl-phenyl

537	2-thienyl(cPr)CH	2-MeO-4-Cl-phenyl
538	3-thienyl(cPr)CH	2-MeO-4-Cl-phenyl
539	2-isoxazolyl(cPr)CH	2-MeO-4-Cl-phenyl
540	2-(5-CH_3-furanyl)(cPr)CH	2-MeO-4-Cl-phenyl
541	2-(4-CH_3-isoxazolyl)(cPr)CH	2-MeO-4-Cl-phenyl
542	cPr-CH(CH_3)	2-MeO-4-Cl-phenyl
543	1-cPr-CH(CH_2CH_3)	2-MeO-4-Cl-phenyl
544	1-cPr-CH($CH_2CH_2CH_3$)	2-MeO-4-Cl-phenyl
545	1-cPr-CH(CH_2OCH_3)	2-MeO-4-Cl-phenyl
546	1-cPr-CH($CH_2CH_2OCH_3$)	2-MeO-4-Cl-phenyl
547	(cBu)$_2$CH	2-MeO-4-Cl-phenyl
548	phenyl(cBu)CH	2-MeO-4-Cl-phenyl
549	2-furanyl(cBu)CH	2-MeO-4-Cl-phenyl
550	3-furan(cBu)CH	2-MeO-4-Cl-phenyl
551	2-thienyl(cBu)CH	2-MeO-4-Cl-phenyl
552	3-thienyl(cBu)CH	2-MeO-4-Cl-phenyl
553	2-isoxazolyl(cBu)CH	2-MeO-4-Cl-phenyl
554	2-(5-CH_3-furanyl)(cBu)CH	2-MeO-4-Cl-phenyl
555	2-(4-CH_3-isoxazolyl)(cBu)CH	2-MeO-4-Cl-phenyl
556	cBu-CH(CH_3)	2-MeO-4-Cl-phenyl
557	1-cBu-CH(CH_2CH_3)	2-MeO-4-Cl-phenyl
558	1-cBu-CH($CH_2CH_2CH_3$)	2-MeO-4-Cl-phenyl
559	1-cBu-CH(CH_2OCH_3)	2-MeO-4-Cl-phenyl
560	1-cBu-CH($CH_2CH_2OCH_3$)	2-MeO-4-Cl-phenyl
561	(cPr)$_2$CH	2,4-diMeO-phenyl
562	phenyl(cPr)CH	2,4-diMeO-phenyl
563	2-furanyl(cPr)CH	2,4-diMeO-phenyl
564	3-furan(cPr)CH	2,4-diMeO-phenyl
565	2-thienyl(cPr)CH	2,4-diMeO-phenyl
566	3-thienyl(cPr)CH	2,4-diMeO-phenyl
567	2-isoxazolyl(cPr)CH	2,4-diMeO-phenyl
568	2-(5-CH_3-furanyl)(cPr)CH	2,4-diMeO-phenyl
569	2-(4-CH_3-isoxazolyl)(cPr)CH	2,4-diMeO-phenyl
570	cPr-CH(CH_3)	2,4-diMeO-phenyl
571	1-cPr-CH(CH_2CH_3)	2,4-diMeO-phenyl
572	1-cPr-CH($CH_2CH_2CH_3$)	2,4-diMeO-phenyl
573	1-cPr-CH(CH_2OCH_3)	2,4-diMeO-phenyl
574	1-cPr-CH($CH_2CH_2OCH_3$)	2,4-diMeO-phenyl

575	$(cBu)_2CH$	2,4-diMeO-phenyl
576	phenyl(cBu)CH	2,4-diMeO-phenyl
577	2-furanyl(cBu)CH	2,4-diMeO-phenyl
578	3-furan(cBu)CH	2,4-diMeO-phenyl
579	2-thienyl(cBu)CH	2,4-diMeO-phenyl
580	3-thienyl(cBu)CH	2,4-diMeO-phenyl
581	2-isoxazolyl(cBu)CH	2,4-diMeO-phenyl
582	2-(5-CH_3-furanyl)(cBu)CH	2,4-diMeO-phenyl
583	2-(4-CH_3-isoxazolyl)(cBu)CH	2,4-diMeO-phenyl
584	cBu-CH(CH_3)	2,4-diMeO-phenyl
585	1-cBu-CH(CH_2CH_3)	2,4-diMeO-phenyl
586	1-cBu-CH($CH_2CH_2CH_3$)	2,4-diMeO-phenyl
587	1-cBu-CH(CH_2OCH_3)	2,4-diMeO-phenyl
588	1-cBu-CH($CH_2CH_2OCH_3$)	2,4-diMeO-phenyl
589	$(cPr)_2CH$	2,4-diCl-6-CH_3-phenyl
590	phenyl(cPr)CH	2,4-diCl-6-CH_3-phenyl
591	2-furanyl(cPr)CH	2,4-diCl-6-CH_3-phenyl
592	3-furan(cPr)CH	2,4-diCl-6-CH_3-phenyl
593	2-thienyl(cPr)CH	2,4-diCl-6-CH_3-phenyl
594	3-thienyl(cPr)CH	2,4-diCl-6-CH_3-phenyl
595	2-isoxazolyl(cPr)CH	2,4-diCl-6-CH_3-phenyl
596	2-(5-CH_3-furanyl)(cPr)CH	2,4-diCl-6-CH_3-phenyl
597	2-(4-CH_3-isoxazolyl)(cPr)CH	2,4-diCl-6-CH_3-phenyl
598	cPr-CH(CH_3)	2,4-diCl-6-CH_3-phenyl
599	1-cPr-CH(CH_2CH_3)	2,4-diCl-6-CH_3-phenyl
600	1-cPr-CH($CH_2CH_2CH_3$)	2,4-diCl-6-CH_3-phenyl
601	1-cPr-CH(CH_2OCH_3)	2,4-diCl-6-CH_3-phenyl
602	1-cPr-CH($CH_2CH_2OCH_3$)	2,4-diCl-6-CH_3-phenyl
603	$(cBu)_2CH$	2,4-diCl-6-CH_3-phenyl
604	phenyl(cBu)CH	2,4-diCl-6-CH_3-phenyl
605	2-furanyl(cBu)CH	2,4-diCl-6-CH_3-phenyl
606	3-furan(cBu)CH	2,4-diCl-6-CH_3-phenyl
607	2-thienyl(cBu)CH	2,4-diCl-6-CH_3-phenyl
608	3-thienyl(cBu)CH	2,4-diCl-6-CH_3-phenyl
609	2-isoxazolyl(cBu)CH	2,4-diCl-6-CH_3-phenyl
610	2-(5-CH_3-furanyl)(cBu)CH	2,4-diCl-6-CH_3-phenyl
611	2-(4-CH_3-isoxazolyl)(cBu)CH	2,4-diCl-6-CH_3-phenyl
612	cBu-CH(CH_3)	2,4-diCl-6-CH_3-phenyl

613	1-cBu-CH(CH_2CH_3)	2,4-diCl-6-CH_3-phenyl
614	1-cBu-CH($CH_2CH_2CH_3$)	2,4-diCl-6-CH_3-phenyl
615	1-cBu-CH(CH_2OCH_3)	2,4-diCl-6-CH_3-phenyl
616	1-cBu-CH($CH_2CH_2OCH_3$)	2,4-diCl-6-CH_3-phenyl
617	(cPr)$_2$CH	2,4-diCl-5-F-phenyl
618	phenyl(cPr)CH	2,4-diCl-5-F-phenyl
619	2-furanyl(cPr)CH	2,4-diCl-5-F-phenyl
620	3-furan(cPr)CH	2,4-diCl-5-F-phenyl
621	2-thienyl(cPr)CH	2,4-diCl-5-F-phenyl
622	3-thienyl(cPr)CH	2,4-diCl-5-F-phenyl
623	2-isoxazolyl(cPr)CH	2,4-diCl-5-F-phenyl
624	2-(5-CH_3-furanyl)(cPr)CH	2,4-diCl-5-F-phenyl
625	2-(4-CH_3-isoxazolyl)(cPr)CH	2,4-diCl-5-F-phenyl
626	cPr-CH(CH_3)	2,4-diCl-5-F-phenyl
627	1-cPr-CH(CH_2CH_3)	2,4-diCl-5-F-phenyl
628	1-cPr-CH($CH_2CH_2CH_3$)	2,4-diCl-5-F-phenyl
629	1-cPr-CH(CH_2OCH_3)	2,4-diCl-5-F-phenyl
630	1-cPr-CH($CH_2CH_2OCH_3$)	2,4-diCl-5-F-phenyl
631	(cBu)$_2$CH	2,4-diCl-5-F-phenyl
632	phenyl(cBu)CH	2,4-diCl-5-F-phenyl
633	2-furanyl(cBu)CH	2,4-diCl-5-F-phenyl
634	3-furan(cBu)CH	2,4-diCl-5-F-phenyl
635	2-thienyl(cBu)CH	2,4-diCl-5-F-phenyl
636	3-thienyl(cBu)CH	2,4-diCl-5-F-phenyl
637	2-isoxazolyl(cBu)CH	2,4-diCl-5-F-phenyl
638	2-(5-CH_3-furanyl)(cBu)CH	2,4-diCl-5-F-phenyl
639	2-(4-CH_3-isoxazolyl)(cBu)CH	2,4-diCl-5-F-phenyl
640	cBu-CH(CH_3)	2,4-diCl-5-F-phenyl
641	1-cBu-CH(CH_2CH_3)	2,4-diCl-5-F-phenyl
642	1-cBu-CH($CH_2CH_2CH_3$)	2,4-diCl-5-F-phenyl
643	1-cBu-CH(CH_2OCH_3)	2,4-diCl-5-F-phenyl
644	1-cBu-CH($CH_2CH_2OCH_3$)	2,4-diCl-5-F-phenyl
645	(cPr)$_2$CH	2,4-diCl-6-MeS-phenyl
646	phenyl(cPr)CH	2,4-diCl-6-MeS-phenyl
647	2-furanyl(cPr)CH	2,4-diCl-6-MeS-phenyl
648	3-furan(cPr)CH	2,4-diCl-6-MeS-phenyl
649	2-thienyl(cPr)CH	2,4-diCl-6-MeS-phenyl
650	3-thienyl(cPr)CH	2,4-diCl-6-MeS-phenyl

651	2-isoxazolyl(cPr)CH	2,4-diCl-6-MeS-phenyl
652	2-(5-CH_3-furanyl)(cPr)CH	2,4-diCl-6-MeS-phenyl
653	2-(4-CH_3-isoxazolyl)(cPr)CH	2,4-diCl-6-MeS-phenyl
654	cPr-$CH(CH_3)$	2,4-diCl-6-MeS-phenyl
655	1-cPr-$CH(CH_2CH_3)$	2,4-diCl-6-MeS-phenyl
656	1-cPr-$CH(CH_2CH_2CH_3)$	2,4-diCl-6-MeS-phenyl
657	1-cPr-$CH(CH_2OCH_3)$	2,4-diCl-6-MeS-phenyl
658	1-cPr-$CH(CH_2CH_2OCH_3)$	2,4-diCl-6-MeS-phenyl
659	$(cBu)_2CH$	2,4-diCl-6-MeS-phenyl
660	phenyl(cBu)CH	2,4-diCl-6-MeS-phenyl
661	2-furanyl(cBu)CH	2,4-diCl-6-MeS-phenyl
662	3-furan(cBu)CH	2,4-diCl-6-MeS-phenyl
663	2-thienyl(cBu)CH	2,4-diCl-6-MeS-phenyl
664	3-thienyl(cBu)CH	2,4-diCl-6-MeS-phenyl
665	2-isoxazolyl(cBu)CH	2,4-diCl-6-MeS-phenyl
666	2-(5-CH_3-furanyl)(cBu)CH	2,4-diCl-6-MeS-phenyl
667	2-(4-CH_3-isoxazolyl)(cBu)CH	2,4-diCl-6-MeS-phenyl
668	cBu-$CH(CH_3)$	2,4-diCl-6-MeS-phenyl
669	1-cBu-$CH(CH_2CH_3)$	2,4-diCl-6-MeS-phenyl
670	1-cBu-$CH(CH_2CH_2CH_3)$	2,4-diCl-6-MeS-phenyl
671	1-cBu-$CH(CH_2OCH_3)$	2,4-diCl-6-MeS-phenyl
672	1-cBu-$CH(CH_2CH_2OCH_3)$	2,4-diCl-6-MeS-phenyl
673	$(cPr)_2CH$	2,4-diCl-6-MeO-phenyl
674	phenyl(cPr)CH	2,4-diCl-6-MeO-phenyl
675	2-furanyl(cPr)CH	2,4-diCl-6-MeO-phenyl
676	3-furan(cPr)CH	2,4-diCl-6-MeO-phenyl
677	2-thienyl(cPr)CH	2,4-diCl-6-MeO-phenyl
678	3-thienyl(cPr)CH	2,4-diCl-6-MeO-phenyl
679	2-isoxazolyl(cPr)CH	2,4-diCl-6-MeO-phenyl
680	2-(5-CH_3-furanyl)(cPr)CH	2,4-diCl-6-MeO-phenyl
681	2-(4-CH_3-isoxazolyl)(cPr)CH	2,4-diCl-6-MeO-phenyl
682	cPr-$CH(CH_3)$	2,4-diCl-6-MeO-phenyl
683	1-cPr-$CH(CH_2CH_3)$	2,4-diCl-6-MeO-phenyl
684	1-cPr-$CH(CH_2CH_2CH_3)$	2,4-diCl-6-MeO-phenyl
685	1-cPr-$CH(CH_2OCH_3)$	2,4-diCl-6-MeO-phenyl
686	1-cPr-$CH(CH_2CH_2OCH_3)$	2,4-diCl-6-MeO-phenyl
687	$(cBu)_2CH$	2,4-diCl-6-MeO-phenyl
688	phenyl(cBu)CH	2,4-diCl-6-MeO-phenyl

689	2-furanyl(cBu)CH	2,4-diCl-6-MeO-phenyl
690	3-furan(cBu)CH	2,4-diCl-6-MeO-phenyl
691	2-thienyl(cBu)CH	2,4-diCl-6-MeO-phenyl
692	3-thienyl(cBu)CH	2,4-diCl-6-MeO-phenyl
693	2-isoxazolyl(cBu)CH	2,4-diCl-6-MeO-phenyl
694	2-(5-CH_3-furanyl)(cBu)CH	2,4-diCl-6-MeO-phenyl
695	2-(4-CH_3-isoxazolyl)(cBu)CH	2,4-diCl-6-MeO-phenyl
696	cBu-CH(CH_3)	2,4-diCl-6-MeO-phenyl
697	1-cBu-CH(CH_2CH_3)	2,4-diCl-6-MeO-phenyl
698	1-cBu-CH($CH_2CH_2CH_3$)	2,4-diCl-6-MeO-phenyl
699	1-cBu-CH(CH_2OCH_3)	2,4-diCl-6-MeO-phenyl
700	1-cBu-CH($CH_2CH_2OCH_3$)	2,4-diCl-6-MeO-phenyl
701	(cPr)$_2$CH	2,5-diCl-4-MeO-phenyl
702	phenyl(cPr)CH	2,5-diCl-4-MeO-phenyl
703	2-furanyl(cPr)CH	2,5-diCl-4-MeO-phenyl
704	3-furan(cPr)CH	2,5-diCl-4-MeO-phenyl
705	2-thienyl(cPr)CH	2,5-diCl-4-MeO-phenyl
706	3-thienyl(cPr)CH	2,5-diCl-4-MeO-phenyl
707	2-isoxazolyl(cPr)CH	2,5-diCl-4-MeO-phenyl
708	2-(5-CH_3-furanyl)(cPr)CH	2,5-diCl-4-MeO-phenyl
709	2-(4-CH_3-isoxazolyl)(cPr)CH	2,5-diCl-4-MeO-phenyl
710	cPr-CH(CH_3)	2,5-diCl-4-MeO-phenyl
711	1-cPr-CH(CH_2CH_3)	2,5-diCl-4-MeO-phenyl
712	1-cPr-CH($CH_2CH_2CH_3$)	2,5-diCl-4-MeO-phenyl
713	1-cPr-CH(CH_2OCH_3)	2,5-diCl-4-MeO-phenyl
714	1-cPr-CH($CH_2CH_2OCH_3$)	2,5-diCl-4-MeO-phenyl
715	(cBu)$_2$CH	2,5-diCl-4-MeO-phenyl
716	phenyl(cBu)CH	2,5-diCl-4-MeO-phenyl
717	2-furanyl(cBu)CH	2,5-diCl-4-MeO-phenyl
718	3-furan(cBu)CH	2,5-diCl-4-MeO-phenyl
719	2-thienyl(cBu)CH	2,5-diCl-4-MeO-phenyl
720	3-thienyl(cBu)CH	2,5-diCl-4-MeO-phenyl
721	2-isoxazolyl(cBu)CH	2,5-diCl-4-MeO-phenyl
722	2-(5-CH_3-furanyl)(cBu)CH	2,5-diCl-4-MeO-phenyl
723	2-(4-CH_3-isoxazolyl)(cBu)CH	2,5-diCl-4-MeO-phenyl
724	cBu-CH(CH_3)	2,5-diCl-4-MeO-phenyl
725	1-cBu-CH(CH_2CH_3)	2,5-diCl-4-MeO-phenyl
726	1-cBu-CH($CH_2CH_2CH_3$)	2,5-diCl-4-MeO-phenyl

727	1-cBu-CH(CH_2OCH_3)	2,5-diCl-4-MeO-phenyl
728	1-cBu-CH($CH_2CH_2OCH_3$)	2,5-diCl-4-MeO-phenyl
729	(cPr)$_2$CH	2,4,6-triCl-phenyl
730	phenyl(cPr)CH	2,4,6-triCl-phenyl
731	2-furanyl(cPr)CH	2,4,6-triCl-phenyl
732	3-furan(cPr)CH	2,4,6-triCl-phenyl
733	2-thienyl(cPr)CH	2,4,6-triCl-phenyl
734	3-thienyl(cPr)CH	2,4,6-triCl-phenyl
735	2-isoxazolyl(cPr)CH	2,4,6-triCl-phenyl
736	2-(5-CH_3-furanyl)(cPr)CH	2,4,6-triCl-phenyl
737	2-(4-CH_3-isoxazolyl)(cPr)CH	2,4,6-triCl-phenyl
738	cPr-CH(CH_3)	2,4,6-triCl-phenyl
739	1-cPr-CH(CH_2CH_3)	2,4,6-triCl-phenyl
740	1-cPr-CH($CH_2CH_2CH_3$)	2,4,6-triCl-phenyl
741	1-cPr-CH(CH_2OCH_3)	2,4,6-triCl-phenyl
742	1-cPr-CH($CH_2CH_2OCH_3$)	2,4,6-triCl-phenyl
743	(cBu)$_2$CH	2,4,6-triCl-phenyl
744	phenyl(cBu)CH	2,4,6-triCl-phenyl
745	2-furanyl(cBu)CH	2,4,6-triCl-phenyl
746	3-furan(cBu)CH	2,4,6-triCl-phenyl
747	2-thienyl(cBu)CH	2,4,6-triCl-phenyl
748	3-thienyl(cBu)CH	2,4,6-triCl-phenyl
749	2-isoxazolyl(cBu)CH	2,4,6-triCl-phenyl
750	2-(5-CH_3-furanyl)(cBu)CH	2,4,6-triCl-phenyl
751	2-(4-CH_3-isoxazolyl)(cBu)CH	2,4,6-triCl-phenyl
752	cBu-CH(CH_3)	2,4,6-triCl-phenyl
753	1-cBu-CH(CH_2CH_3)	2,4,6-triCl-phenyl
754	1-cBu-CH($CH_2CH_2CH_3$)	2,4,6-triCl-phenyl
755	1-cBu-CH(CH_2OCH_3)	2,4,6-triCl-phenyl
756	1-cBu-CH($CH_2CH_2OCH_3$)	2,4,6-triCl-phenyl
757	(cPr)$_2$CH	2-Cl-4-CH_3-5-F-phenyl
758	phenyl(cPr)CH	2-Cl-4-CH_3-5-F-phenyl
759	2-furanyl(cPr)CH	2-Cl-4-CH_3-5-F-phenyl
760	3-furan(cPr)CH	2-Cl-4-CH_3-5-F-phenyl
761	2-thienyl(cPr)CH	2-Cl-4-CH_3-5-F-phenyl
762	3-thienyl(cPr)CH	2-Cl-4-CH_3-5-F-phenyl
763	2-isoxazolyl(cPr)CH	2-Cl-4-CH_3-5-F-phenyl
764	2-(5-CH_3-furanyl)(cPr)CH	2-Cl-4-CH_3-5-F-phenyl

765	2-(4-CH_3-isoxazolyl)(cPr)CH	2-Cl-4-CH_3-5-F-phenyl
766	cPr-CH(CH_3)	2-Cl-4-CH_3-5-F-phenyl
767	1-cPr-CH(CH_2CH_3)	2-Cl-4-CH_3-5-F-phenyl
768	1-cPr-CH($CH_2CH_2CH_3$)	2-Cl-4-CH_3-5-F-phenyl
769	1-cPr-CH(CH_2OCH_3)	2-Cl-4-CH_3-5-F-phenyl
770	1-cPr-CH($CH_2CH_2OCH_3$)	2-Cl-4-CH_3-5-F-phenyl
771	(cBu)$_2$CH	2-Cl-4-CH_3-5-F-phenyl
772	phenyl(cBu)CH	2-Cl-4-CH_3-5-F-phenyl
773	2-furanyl(cBu)CH	2-Cl-4-CH_3-5-F-phenyl
774	3-furan(cBu)CH	2-Cl-4-CH_3-5-F-phenyl
775	2-thienyl(cBu)CH	2-Cl-4-CH_3-5-F-phenyl
776	3-thienyl(cBu)CH	2-Cl-4-CH_3-5-F-phenyl
777	2-isoxazolyl(cBu)CH	2-Cl-4-CH_3-5-F-phenyl
778	2-(5-CH_3-furanyl)(cBu)CH	2-Cl-4-CH_3-5-F-phenyl
779	2-(4-CH_3-isoxazolyl)(cBu)CH	2-Cl-4-CH_3-5-F-phenyl
780	cBu-CH(CH_3)	2-Cl-4-CH_3-5-F-phenyl
781	1-cBu-CH(CH_2CH_3)	2-Cl-4-CH_3-5-F-phenyl
782	1-cBu-CH($CH_2CH_2CH_3$)	2-Cl-4-CH_3-5-F-phenyl
783	1-cBu-CH(CH_2OCH_3)	2-Cl-4-CH_3-5-F-phenyl
784	1-cBu-CH($CH_2CH_2OCH_3$)	2-Cl-4-CH_3-5-F-phenyl
785	(cPr)$_2$CH	2-Cl-4-MeO-5-CH_3-phenyl
786	phenyl(cPr)CH	2-Cl-4-MeO-5-CH_3-phenyl
787	2-furanyl(cPr)CH	2-Cl-4-MeO-5-CH_3-phenyl
788	3-furan(cPr)CH	2-Cl-4-MeO-5-CH_3-phenyl
789	2-thienyl(cPr)CH	2-Cl-4-MeO-5-CH_3-phenyl
790	3-thienyl(cPr)CH	2-Cl-4-MeO-5-CH_3-phenyl
791	2-isoxazolyl(cPr)CH	2-Cl-4-MeO-5-CH_3-phenyl
792	2-(5-CH_3-furanyl)(cPr)CH	2-Cl-4-MeO-5-CH_3-phenyl
793	2-(4-CH_3-isoxazolyl)(cPr)CH	2-Cl-4-MeO-5-CH_3-phenyl
794	cPr-CH(CH_3)	2-Cl-4-MeO-5-CH_3-phenyl
795	1-cPr-CH(CH_2CH_3)	2-Cl-4-MeO-5-CH_3-phenyl
796	1-cPr-CH($CH_2CH_2CH_3$)	2-Cl-4-MeO-5-CH_3-phenyl
797	1-cPr-CH(CH_2OCH_3)	2-Cl-4-MeO-5-CH_3-phenyl
798	1-cPr-CH($CH_2CH_2OCH_3$)	2-Cl-4-MeO-5-CH_3-phenyl
799	(cBu)$_2$CH	2-Cl-4-MeO-5-CH_3-phenyl
800	phenyl(cBu)CH	2-Cl-4-MeO-5-CH_3-phenyl
801	2-furanyl(cBu)CH	2-Cl-4-MeO-5-CH_3-phenyl
802	3-furan(cBu)CH	2-Cl-4-MeO-5-CH_3-phenyl

803	2-thienyl(cBu)CH	2-Cl-4-MeO-5-CH_3-phenyl
804	3-thienyl(cBu)CH	2-Cl-4-MeO-5-CH_3-phenyl
805	2-isoxazolyl(cBu)CH	2-Cl-4-MeO-5-CH_3-phenyl
806	2-(5-CH_3-furanyl)(cBu)CH	2-Cl-4-MeO-5-CH_3-phenyl
807	2-(4-CH_3-isoxazolyl)(cBu)CH	2-Cl-4-MeO-5-CH_3-phenyl
808	cBu-CH(CH_3)	2-Cl-4-MeO-5-CH_3-phenyl
809	1-cBu-CH(CH_2CH_3)	2-Cl-4-MeO-5-CH_3-phenyl
810	1-cBu-CH($CH_2CH_2CH_3$)	2-Cl-4-MeO-5-CH_3-phenyl
811	1-cBu-CH(CH_2OCH_3)	2-Cl-4-MeO-5-CH_3-phenyl
812	1-cBu-CH($CH_2CH_2OCH_3$)	2-Cl-4-MeO-5-CH_3-phenyl
813	(cPr)$_2$CH	2-Cl-4-MeO-5-F-phenyl
814	phenyl(cPr)CH	2-Cl-4-MeO-5-F-phenyl
815	2-furanyl(cPr)CH	2-Cl-4-MeO-5-F-phenyl
816	3-furan(cPr)CH	2-Cl-4-MeO-5-F-phenyl
817	2-thienyl(cPr)CH	2-Cl-4-MeO-5-F-phenyl
818	3-thienyl(cPr)CH	2-Cl-4-MeO-5-F-phenyl
819	2-isoxazolyl(cPr)CH	2-Cl-4-MeO-5-F-phenyl
820	2-(5-CH_3-furanyl)(cPr)CH	2-Cl-4-MeO-5-F-phenyl
821	2-(4-CH_3-isoxazolyl)(cPr)CH	2-Cl-4-MeO-5-F-phenyl
822	cPr-CH(CH_3)	2-Cl-4-MeO-5-F-phenyl
823	1-cPr-CH(CH_2CH_3)	2-Cl-4-MeO-5-F-phenyl
824	1-cPr-CH($CH_2CH_2CH_3$)	2-Cl-4-MeO-5-F-phenyl
825	1-cPr-CH(CH_2OCH_3)	2-Cl-4-MeO-5-F-phenyl
826	1-cPr-CH($CH_2CH_2OCH_3$)	2-Cl-4-MeO-5-F-phenyl
827	(cBu)$_2$CH	2-Cl-4-MeO-5-F-phenyl
828	phenyl(cBu)CH	2-Cl-4-MeO-5-F-phenyl
829	2-furanyl(cBu)CH	2-Cl-4-MeO-5-F-phenyl
830	3-furan(cBu)CH	2-Cl-4-MeO-5-F-phenyl
831	2-thienyl(cBu)CH	2-Cl-4-MeO-5-F-phenyl
832	3-thienyl(cBu)CH	2-Cl-4-MeO-5-F-phenyl
833	2-isoxazolyl(cBu)CH	2-Cl-4-MeO-5-F-phenyl
834	2-(5-CH_3-furanyl)(cBu)CH	2-Cl-4-MeO-5-F-phenyl
835	2-(4-CH_3-isoxazolyl)(cBu)CH	2-Cl-4-MeO-5-F-phenyl
836	cBu-CH(CH_3)	2-Cl-4-MeO-5-F-phenyl
837	1-cBu-CH(CH_2CH_3)	2-Cl-4-MeO-5-F-phenyl
838	1-cBu-CH($CH_2CH_2CH_3$)	2-Cl-4-MeO-5-F-phenyl
839	1-cBu-CH(CH_2OCH_3)	2-Cl-4-MeO-5-F-phenyl
840	1-cBu-CH($CH_2CH_2OCH_3$)	2-Cl-4-MeO-5-F-phenyl

841	(cPr)$_2$CH	2-CH$_3$-4-MeO-5-Cl-phenyl
842	phenyl(cPr)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
843	2-furanyl(cPr)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
844	3-furan(cPr)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
845	2-thienyl(cPr)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
846	3-thienyl(cPr)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
847	2-isoxazolyl(cPr)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
848	2-(5-CH$_3$-furanyl)(cPr)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
849	2-(4-CH$_3$-isoxazolyl)(cPr)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
850	cPr-CH(CH$_3$)	2-CH$_3$-4-MeO-5-Cl-phenyl
851	1-cPr-CH(CH$_2$CH$_3$)	2-CH$_3$-4-MeO-5-Cl-phenyl
852	1-cPr-CH(CH$_2$CH$_2$CH$_3$)	2-CH$_3$-4-MeO-5-Cl-phenyl
853	1-cPr-CH(CH$_2$OCH$_3$)	2-CH$_3$-4-MeO-5-Cl-phenyl
854	1-cPr-CH(CH$_2$CH$_2$OCH$_3$)	2-CH$_3$-4-MeO-5-Cl-phenyl
855	(cBu)$_2$CH	2-CH$_3$-4-MeO-5-Cl-phenyl
856	phenyl(cBu)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
857	2-furanyl(cBu)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
858	3-furan(cBu)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
859	2-thienyl(cBu)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
860	3-thienyl(cBu)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
861	2-isoxazolyl(cBu)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
862	2-(5-CH$_3$-furanyl)(cBu)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
863	2-(4-CH$_3$-isoxazolyl)(cBu)CH	2-CH$_3$-4-MeO-5-Cl-phenyl
864	cBu-CH(CH$_3$)	2-CH$_3$-4-MeO-5-Cl-phenyl
865	1-cBu-CH(CH$_2$CH$_3$)	2-CH$_3$-4-MeO-5-Cl-phenyl
866	1-cBu-CH(CH$_2$CH$_2$CH$_3$)	2-CH$_3$-4-MeO-5-Cl-phenyl
867	1-cBu-CH(CH$_2$OCH$_3$)	2-CH$_3$-4-MeO-5-Cl-phenyl
868	1-cBu-CH(CH$_2$CH$_2$OCH$_3$)	2-CH$_3$-4-MeO-5-Cl-phenyl
869	(cPr)$_2$CH	2,5-diCH$_3$-4-MeO-phenyl
870	phenyl(cPr)CH	2,5-diCH$_3$-4-MeO-phenyl
871	2-furanyl(cPr)CH	2,5-diCH$_3$-4-MeO-phenyl
872	3-furan(cPr)CH	2,5-diCH$_3$-4-MeO-phenyl
873	2-thienyl(cPr)CH	2,5-diCH$_3$-4-MeO-phenyl
874	3-thienyl(cPr)CH	2,5-diCH$_3$-4-MeO-phenyl
875	2-isoxazolyl(cPr)CH	2,5-diCH$_3$-4-MeO-phenyl
876	2-(5-CH$_3$-furanyl)(cPr)CH	2,5-diCH$_3$-4-MeO-phenyl
877	2-(4-CH$_3$-isoxazolyl)(cPr)CH	2,5-diCH$_3$-4-MeO-phenyl
878	cPr-CH(CH$_3$)	2,5-diCH$_3$-4-MeO-phenyl

879	1-cPr-CH(CH_2CH_3)	2,5-diCH_3-4-MeO-phenyl
880	1-cPr-CH($CH_2CH_2CH_3$)	2,5-diCH_3-4-MeO-phenyl
881	1-cPr-CH(CH_2OCH_3)	2,5-diCH_3-4-MeO-phenyl
882	1-cPr-CH($CH_2CH_2OCH_3$)	2,5-diCH_3-4-MeO-phenyl
883	(cBu)$_2$CH	2,5-diCH_3-4-MeO-phenyl
884	phenyl(cBu)CH	2,5-diCH_3-4-MeO-phenyl
885	2-furanyl(cBu)CH	2,5-diCH_3-4-MeO-phenyl
886	3-furan(cBu)CH	2,5-diCH_3-4-MeO-phenyl
887	2-thienyl(cBu)CH	2,5-diCH_3-4-MeO-phenyl
888	3-thienyl(cBu)CH	2,5-diCH_3-4-MeO-phenyl
889	2-isoxazolyl(cBu)CH	2,5-diCH_3-4-MeO-phenyl
890	2-(5-CH_3-furanyl)(cBu)CH	2,5-diCH_3-4-MeO-phenyl
891	2-(4-CH_3-isoxazolyl)(cBu)CH	2,5-diCH_3-4-MeO-phenyl
892	cBu-CH(CH_3)	2,5-diCH_3-4-MeO-phenyl
893	1-cBu-CH(CH_2CH_3)	2,5-diCH_3-4-MeO-phenyl
894	1-cBu-CH($CH_2CH_2CH_3$)	2,5-diCH_3-4-MeO-phenyl
895	1-cBu-CH(CH_2OCH_3)	2,5-diCH_3-4-MeO-phenyl
896	1-cBu-CH($CH_2CH_2OCH_3$)	2,5-diCH_3-4-MeO-phenyl
897	(cPr)$_2$CH	2-CH_3-4-MeO-5-F-phenyl
898	phenyl(cPr)CH	2-CH_3-4-MeO-5-F-phenyl
899	2-furanyl(cPr)CH	2-CH_3-4-MeO-5-F-phenyl
900	3-furan(cPr)CH	2-CH_3-4-MeO-5-F-phenyl
901	2-thienyl(cPr)CH	2-CH_3-4-MeO-5-F-phenyl
902	3-thienyl(cPr)CH	2-CH_3-4-MeO-5-F-phenyl
903	2-isoxazolyl(cPr)CH	2-CH_3-4-MeO-5-F-phenyl
904	2-(5-CH_3-furanyl)(cPr)CH	2-CH_3-4-MeO-5-F-phenyl
905	2-(4-CH_3-isoxazolyl)(cPr)CH	2-CH_3-4-MeO-5-F-phenyl
906	cPr-CH(CH_3)	2-CH_3-4-MeO-5-F-phenyl
907	1-cPr-CH(CH_2CH_3)	2-CH_3-4-MeO-5-F-phenyl
908	1-cPr-CH($CH_2CH_2CH_3$)	2-CH_3-4-MeO-5-F-phenyl
909	1-cPr-CH(CH_2OCH_3)	2-CH_3-4-MeO-5-F-phenyl
910	1-cPr-CH($CH_2CH_2OCH_3$)	2-CH_3-4-MeO-5-F-phenyl
911	(cBu)$_2$CH	2-CH_3-4-MeO-5-F-phenyl
912	phenyl(cBu)CH	2-CH_3-4-MeO-5-F-phenyl
913	2-furanyl(cBu)CH	2-CH_3-4-MeO-5-F-phenyl
914	3-furan(cBu)CH	2-CH_3-4-MeO-5-F-phenyl
915	2-thienyl(cBu)CH	2-CH_3-4-MeO-5-F-phenyl
916	3-thienyl(cBu)CH	2-CH_3-4-MeO-5-F-phenyl

	917	2-isoxazolyl(cBu)CH	2-CH_3-4-MeO-5-F-phenyl
	918	2-(5-CH_3-furanyl)(cBu)CH	2-CH_3-4-MeO-5-F-phenyl
	919	2-(4-CH_3-isoxazolyl)(cBu)CH	2-CH_3-4-MeO-5-F-phenyl
	920	cBu-CH(CH_3)	2-CH_3-4-MeO-5-F-phenyl
5	921	1-cBu-CH(CH_2CH_3)	2-CH_3-4-MeO-5-F-phenyl
	922	1-cBu-CH($CH_2CH_2CH_3$)	2-CH_3-4-MeO-5-F-phenyl
	923	1-cBu-CH(CH_2OCH_3)	2-CH_3-4-MeO-5-F-phenyl
	924	1-cBu-CH($CH_2CH_2OCH_3$)	2-CH_3-4-MeO-5-F-phenyl
	925	(cPr)$_2$CH	2,4,6-triCH_3-phenyl
10	926	phenyl(cPr)CH	2,4,6-triCH_3-phenyl
	927	2-furanyl(cPr)CH	2,4,6-triCH_3-phenyl
	928	3-furan(cPr)CH	2,4,6-triCH_3-phenyl
	929	2-thienyl(cPr)CH	2,4,6-triCH_3-phenyl
	930	3-thienyl(cPr)CH	2,4,6-triCH_3-phenyl
15	931	2-isoxazolyl(cPr)CH	2,4,6-triCH_3-phenyl
	932	2-(5-CH_3-furanyl)(cPr)CH	2,4,6-triCH_3-phenyl
	933	2-(4-CH_3-isoxazolyl)(cPr)CH	2,4,6-triCH_3-phenyl
	934	cPr-CH(CH_3)	2,4,6-triCH_3-phenyl
	935	1-cPr-CH(CH_2CH_3)	2,4,6-triCH_3-phenyl
20	936	1-cPr-CH($CH_2CH_2CH_3$)	2,4,6-triCH_3-phenyl
	937	1-cPr-CH(CH_2OCH_3)	2,4,6-triCH_3-phenyl
	938	1-cPr-CH($CH_2CH_2OCH_3$)	2,4,6-triCH_3-phenyl
	939	(cBu)$_2$CH	2,4,6-triCH_3-phenyl
	940	phenyl(cBu)CH	2,4,6-triCH_3-phenyl
25	941	2-furanyl(cBu)CH	2,4,6-triCH_3-phenyl
	942	3-furan(cBu)CH	2,4,6-triCH_3-phenyl
	943	2-thienyl(cBu)CH	2,4,6-triCH_3-phenyl
	944	3-thienyl(cBu)CH	2,4,6-triCH_3-phenyl
	945	2-isoxazolyl(cBu)CH	2,4,6-triCH_3-phenyl
30	946	2-(5-CH_3-furanyl)(cBu)CH	2,4,6-triCH_3-phenyl
	947	2-(4-CH_3-isoxazolyl)(cBu)CH	2,4,6-triCH_3-phenyl
	948	cBu-CH(CH_3)	2,4,6-triCH_3-phenyl
	949	1-cBu-CH(CH_2CH_3)	2,4,6-triCH_3-phenyl
	950	1-cBu-CH($CH_2CH_2CH_3$)	2,4,6-triCH_3-phenyl
35	951	1-cBu-CH(CH_2OCH_3)	2,4,6-triCH_3-phenyl
	952	1-cBu-CH($CH_2CH_2OCH_3$)	2,4,6-triCH_3-phenyl

	953	$(cPr)_2CH$	3-pyridyl
	954	phenyl(cPr)CH	3-pyridyl
	955	2-furanyl(cPr)CH	3-pyridyl
	956	3-furan(cPr)CH	3-pyridyl
5	957	2-thienyl(cPr)CH	3-pyridyl
	958	3-thienyl(cPr)CH	3-pyridyl
	959	2-isoxazolyl(cPr)CH	3-pyridyl
	960	2-(5-CH_3-furanyl)(cPr)CH	3-pyridyl
	961	2-(4-CH_3-isoxazolyl)(cPr)CH	3-pyridyl
10	962	cPr-CH(CH_3)	3-pyridyl
	963	1-cPr-CH(CH_2CH_3)	3-pyridyl
	964	1-cPr-CH($CH_2CH_2CH_3$)	3-pyridyl
	965	1-cPr-CH(CH_2OCH_3)	3-pyridyl
	966	1-cPr-CH($CH_2CH_2OCH_3$)	3-pyridyl
15	967	$(cBu)_2CH$	3-pyridyl
	968	phenyl(cBu)CH	3-pyridyl
	969	2-furanyl(cBu)CH	3-pyridyl
	970	3-furan(cBu)CH	3-pyridyl
	971	2-thienyl(cBu)CH	3-pyridyl
20	972	3-thienyl(cBu)CH	3-pyridyl
	973	2-isoxazolyl(cBu)CH	3-pyridyl
	974	2-(5-CH_3-furanyl)(cBu)CH	3-pyridyl
	975	2-(4-CH_3-isoxazolyl)(cBu)CH	3-pyridyl
	976	cBu-CH(CH_3)	3-pyridyl
25	977	1-cBu-CH(CH_2CH_3)	3-pyridyl
	978	1-cBu-CH($CH_2CH_2CH_3$)	3-pyridyl
	979	1-cBu-CH(CH_2OCH_3)	3-pyridyl
	980	1-cBu-CH($CH_2CH_2OCH_3$)	3-pyridyl
	981	$(cPr)_2CH$	2,6-diMeO-pyrid-3-yl
30	982	phenyl(cPr)CH	2,6-diMeO-pyrid-3-yl
	983	2-furanyl(cPr)CH	2,6-diMeO-pyrid-3-yl
	984	3-furan(cPr)CH	2,6-diMeO-pyrid-3-yl
	985	2-thienyl(cPr)CH	2,6-diMeO-pyrid-3-yl
	986	3-thienyl(cPr)CH	2,6-diMeO-pyrid-3-yl
35	987	2-isoxazolyl(cPr)CH	2,6-diMeO-pyrid-3-yl
	988	2-(5-CH_3-furanyl)(cPr)CH	2,6-diMeO-pyrid-3-yl
	989	2-(4-CH_3-isoxazolyl)(cPr)CH	2,6-diMeO-pyrid-3-yl
	990	cPr-CH(CH_3)	2,6-diMeO-pyrid-3-yl

	991	1-cPr-CH(CH_2CH_3)	2,6-diMeO-pyrid-3-yl
	992	1-cPr-CH($CH_2CH_2CH_3$)	2,6-diMeO-pyrid-3-yl
	993	1-cPr-CH(CH_2OCH_3)	2,6-diMeO-pyrid-3-yl
	994	1-cPr-CH($CH_2CH_2OCH_3$)	2,6-diMeO-pyrid-3-yl
5	995	(cBu)$_2$CH	2,6-diMeO-pyrid-3-yl
	996	phenyl(cBu)CH	2,6-diMeO-pyrid-3-yl
	997	2-furanyl(cBu)CH	2,6-diMeO-pyrid-3-yl
	998	3-furan(cBu)CH	2,6-diMeO-pyrid-3-yl
	999	2-thienyl(cBu)CH	2,6-diMeO-pyrid-3-yl
10	1000	3-thienyl(cBu)CH	2,6-diMeO-pyrid-3-yl
	1001	2-isoxazolyl(cBu)CH	2,6-diMeO-pyrid-3-yl
	1002	2-(5-CH_3-furanyl)(cBu)CH	2,6-diMeO-pyrid-3-yl
	1003	2-(4-CH_3-isoxazolyl)(cBu)CH	2,6-diMeO-pyrid-3-yl
	1004	cBu-CH(CH_3)	2,6-diMeO-pyrid-3-yl
15	1005	1-cBu-CH(CH_2CH_3)	2,6-diMeO-pyrid-3-yl
	1006	1-cBu-CH($CH_2CH_2CH_3$)	2,6-diMeO-pyrid-3-yl
	1007	1-cBu-CH(CH_2OCH_3)	2,6-diMeO-pyrid-3-yl
	1008	1-cBu-CH($CH_2CH_2OCH_3$)	2,6-diMeO-pyrid-3-yl
	1009	(cPr)$_2$CH	2,6-diCH3-pyrid-3-yl
20	1010	phenyl(cPr)CH	2,6-diCH3-pyrid-3-yl
	1011	2-furanyl(cPr)CH	2,6-diCH3-pyrid-3-yl
	1012	3-furan(cPr)CH	2,6-diCH3-pyrid-3-yl
	1013	2-thienyl(cPr)CH	2,6-diCH3-pyrid-3-yl
	1014	3-thienyl(cPr)CH	2,6-diCH3-pyrid-3-yl
25	1015	2-isoxazolyl(cPr)CH	2,6-diCH3-pyrid-3-yl
	1016	2-(5-CH_3-furanyl)(cPr)CH	2,6-diCH3-pyrid-3-yl
	1017	2-(4-CH_3-isoxazolyl)(cPr)CH	2,6-diCH3-pyrid-3-yl
	1018	cPr-CH(CH_3)	2,6-diCH3-pyrid-3-yl
	1019	1-cPr-CH(CH_2CH_3)	2,6-diCH3-pyrid-3-yl
30	1020	1-cPr-CH($CH_2CH_2CH_3$)	2,6-diCH3-pyrid-3-yl
	1021	1-cPr-CH(CH_2OCH_3)	2,6-diCH3-pyrid-3-yl
	1022	1-cPr-CH($CH_2CH_2OCH_3$)	2,6-diCH3-pyrid-3-yl
	1023	(cBu)$_2$CH	2,6-diCH3-pyrid-3-yl
	1024	phenyl(cBu)CH	2,6-diCH3-pyrid-3-yl
35	1025	2-furanyl(cBu)CH	2,6-diCH3-pyrid-3-yl
	1026	3-furan(cBu)CH	2,6-diCH3-pyrid-3-yl
	1027	2-thienyl(cBu)CH	2,6-diCH3-pyrid-3-yl
	1028	3-thienyl(cBu)CH	2,6-diCH3-pyrid-3-yl

1029	2-isoxazolyl(cBu)CH	2,6-diCH3-pyrid-3-yl
1030	2-(5-CH3-furanyl)(cBu)CH	2,6-diCH3-pyrid-3-yl
1031	2-(4-CH3-isoxazolyl)(cBu)CH	2,6-diCH3-pyrid-3-yl
1032	cBu-CH(CH3)	2,6-diCH3-pyrid-3-yl
1033	1-cBu-CH(CH2CH3)	2,6-diCH3-pyrid-3-yl
1034	1-cBu-CH(CH2CH2CH3)	2,6-diCH3-pyrid-3-yl
1035	1-cBu-CH(CH2OCH3)	2,6-diCH3-pyrid-3-yl
1036	1-cBu-CH(CH2CH2OCH3)	2,6-diCH3-pyrid-3-yl
1037	(cPr)2CH	2-CH3-6-MeO-pyrid-3-yl
1038	phenyl(cPr)CH	2-CH3-6-MeO-pyrid-3-yl
1039	2-furanyl(cPr)CH	2-CH3-6-MeO-pyrid-3-yl
1040	3-furan(cPr)CH	2-CH3-6-MeO-pyrid-3-yl
1041	2-thienyl(cPr)CH	2-CH3-6-MeO-pyrid-3-yl
1042	3-thienyl(cPr)CH	2-CH3-6-MeO-pyrid-3-yl
1043	2-isoxazolyl(cPr)CH	2-CH3-6-MeO-pyrid-3-yl
1044	2-(5-CH3-furanyl)(cPr)CH	2-CH3-6-MeO-pyrid-3-yl
1045	2-(4-CH3-isoxazolyl)(cPr)CH	2-CH3-6-MeO-pyrid-3-yl
1046	cPr-CH(CH3)	2-CH3-6-MeO-pyrid-3-yl
1047	1-cPr-CH(CH2CH3)	2-CH3-6-MeO-pyrid-3-yl
1048	1-cPr-CH(CH2CH2CH3)	2-CH3-6-MeO-pyrid-3-yl
1049	1-cPr-CH(CH2OCH3)	2-CH3-6-MeO-pyrid-3-yl
1050	1-cPr-CH(CH2CH2OCH3)	2-CH3-6-MeO-pyrid-3-yl
1051	(cBu)2CH	2-CH3-6-MeO-pyrid-3-yl
1052	phenyl(cBu)CH	2-CH3-6-MeO-pyrid-3-yl
1053	2-furanyl(cBu)CH	2-CH3-6-MeO-pyrid-3-yl
1054	3-furan(cBu)CH	2-CH3-6-MeO-pyrid-3-yl
1055	2-thienyl(cBu)CH	2-CH3-6-MeO-pyrid-3-yl
1056	3-thienyl(cBu)CH	2-CH3-6-MeO-pyrid-3-yl
1057	2-isoxazolyl(cBu)CH	2-CH3-6-MeO-pyrid-3-yl
1058	2-(5-CH3-furanyl)(cBu)CH	2-CH3-6-MeO-pyrid-3-yl
1059	2-(4-CH3-isoxazolyl)(cBu)CH	2-CH3-6-MeO-pyrid-3-yl
1060	cBu-CH(CH3)	2-CH3-6-MeO-pyrid-3-yl
1061	1-cBu-CH(CH2CH3)	2-CH3-6-MeO-pyrid-3-yl
1062	1-cBu-CH(CH2CH2CH3)	2-CH3-6-MeO-pyrid-3-yl
1063	1-cBu-CH(CH2OCH3)	2-CH3-6-MeO-pyrid-3-yl
1064	1-cBu-CH(CH2CH2OCH3)	2-CH3-6-MeO-pyrid-3-yl
1065	(cPr)2CH	4-CH3-6-MeO-pyrid-3-yl
1066	phenyl(cPr)CH	4-CH3-6-MeO-pyrid-3-yl

1067	2-furanyl(cPr)CH	4-CH_3-6-MeO-pyrid-3-yl
1068	3-furan(cPr)CH	4-CH_3-6-MeO-pyrid-3-yl
1069	2-thienyl(cPr)CH	4-CH_3-6-MeO-pyrid-3-yl
1070	3-thienyl(cPr)CH	4-CH_3-6-MeO-pyrid-3-yl
1071	2-isoxazolyl(cPr)CH	4-CH_3-6-MeO-pyrid-3-yl
1072	2-(5-CH_3-furanyl)(cPr)CH	4-CH_3-6-MeO-pyrid-3-yl
1073	2-(4-CH_3-isoxazolyl)(cPr)CH	4-CH_3-6-MeO-pyrid-3-yl
1074	cPr-CH(CH_3)	4-CH_3-6-MeO-pyrid-3-yl
1075	1-cPr-CH(CH_2CH_3)	4-CH_3-6-MeO-pyrid-3-yl
1076	1-cPr-CH($CH_2CH_2CH_3$)	4-CH_3-6-MeO-pyrid-3-yl
1077	1-cPr-CH(CH_2OCH_3)	4-CH_3-6-MeO-pyrid-3-yl
1078	1-cPr-CH($CH_2CH_2OCH_3$)	4-CH_3-6-MeO-pyrid-3-yl
1079	(cBu)$_2$CH	4-CH_3-6-MeO-pyrid-3-yl
1080	phenyl(cBu)CH	4-CH_3-6-MeO-pyrid-3-yl
1081	2-furanyl(cBu)CH	4-CH_3-6-MeO-pyrid-3-yl
1082	3-furan(cBu)CH	4-CH_3-6-MeO-pyrid-3-yl
1083	2-thienyl(cBu)CH	4-CH_3-6-MeO-pyrid-3-yl
1084	3-thienyl(cBu)CH	4-CH_3-6-MeO-pyrid-3-yl
1085	2-isoxazolyl(cBu)CH	4-CH_3-6-MeO-pyrid-3-yl
1086	2-(5-CH_3-furanyl)(cBu)CH	4-CH_3-6-MeO-pyrid-3-yl
1087	2-(4-CH_3-isoxazolyl)(cBu)CH	4-CH_3-6-MeO-pyrid-3-yl
1088	cBu-CH(CH_3)	4-CH_3-6-MeO-pyrid-3-yl
1089	1-cBu-CH(CH_2CH_3)	4-CH_3-6-MeO-pyrid-3-yl
1090	1-cBu-CH($CH_2CH_2CH_3$)	4-CH_3-6-MeO-pyrid-3-yl
1091	1-cBu-CH(CH_2OCH_3)	4-CH_3-6-MeO-pyrid-3-yl
1092	1-cBu-CH($CH_2CH_2OCH_3$)	4-CH_3-6-MeO-pyrid-3-yl
1093	(cPr)$_2$CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1094	phenyl(cPr)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1095	2-furanyl(cPr)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1096	3-furan(cPr)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1097	2-thienyl(cPr)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1098	3-thienyl(cPr)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1099	2-isoxazolyl(cPr)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1100	2-(5-CH_3-furanyl)(cPr)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1101	2-(4-CH_3-isoxazolyl)(cPr)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1102	cPr-CH(CH_3)	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1103	1-cPr-CH(CH_2CH_3)	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1104	1-cPr-CH($CH_2CH_2CH_3$)	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl

1105	1-cPr-CH(CH_2OCH_3)	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1106	1-cPr-CH($CH_2CH_2OCH_3$)	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1107	$(cBu)_2CH$	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1108	phenyl(cBu)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1109	2-furanyl(cBu)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1110	3-furan(cBu)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1111	2-thienyl(cBu)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1112	3-thienyl(cBu)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1113	2-isoxazolyl(cBu)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1114	2-(5-CH_3-furanyl)(cBu)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1115	2-(4-CH_3-isoxazolyl)(cBu)CH	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1116	cBu-CH(CH_3)	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1117	1-cBu-CH(CH_2CH_3)	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1118	1-cBu-CH($CH_2CH_2CH_3$)	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1119	1-cBu-CH(CH_2OCH_3)	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1120	1-cBu-CH($CH_2CH_2OCH_3$)	4-CH_3-6-$(CH_3)_2$N-pyrid-3-yl
1121	3-pentyl	2,4,6-$(CH_3)_3$ phenyl
1122	3-pentyl	2,4-Cl_2-5-F-phenyl
1123	3-pentyl	2,4-$(MEO)_2$-phenyl
1124	3-pentyl	2,4-Cl_2-phenyl
1	3-pentyl	2,4-Cl_2-phenyl

Table 1 shows compounds which may readily be prepared according to the procedures described herein in the synthetic schemes and text. The preferred compounds have a core of e_4 with the exception of Examples 95 and 1124, which have cores of c_4 and f_4 respectively. Example 1 has a melting point of 136-138°C.

Utility

Compounds of this invention are expected to have utility in the treatment of inbalances associated with abnormal levels of CRF in patients suffering from depression, affective disorders, and/or anxiety.

CRF-R1 Receptor Binding Assay for the Evaluation of Biological Activity

The following is a description of the isolation of cell membranes containing cloned human CRF-R1 receptors for use in the standard binding assay as well as a description of the assay itself.

Messenger RNA was isolated from human hippocampus. The mRNA was reverse transcribed using oligo (dt) 12-18 and the coding region was amplified by PCR from start to stop codons The resulting PCR fragment was cloned into the EcoRV site of pGEMV, from whence the insert was reclaimed using XhoI + XbaI and cloned into the XhoI + XbaI sites of vector pm3ar (which contains a CMV promoter, the SV40 't' splice and early poly A signals, an Epstein-Barr viral origin of replication, and a hygromycin selectable marker). The resulting expression vector, called phchCRFR was transfected in 293EBNA cells and cells retaining the episome were selected in the presence of 400 µM hygromycin. Cells surviving 4 weeks of selection in hygromycin were pooled, adapted to growth in suspension and used to generate membranes for the binding assay described below. Individual aliquots containing approximately 1 x 10^8 of the suspended cells were then centrifuged to form a pellet and frozen.

For the binding assay a frozen pellet described above containing 293EBNA cells transfected with hCRFR1 receptors is homogenized in 10 ml of ice cold tissue buffer (50 mM HEPES buffer pH 7.0, containing 10 mM $MgCl_2$, 2 mM EGTA, 1 µg/l aprotinin, 1 µg/ml leupeptin and 1 µg/ml pepstatin). The homogenate is centrifuged at 40,000 x g for 12 min and the resulting pellet rehomogenized in 10 ml of tissue buffer. After another centrifugation at 40,000 x g for 12 min, the

pellet is resuspended to a protein concentration of 360 µg/ml to be used in the assay.

Binding assays are performed in 96 well plates; each well having a 300 µl capacity. To each well is added 50 µl of test drug dilutions (final concentration of drugs range from 10^{-10} - 10^{-5} M), 100 µl of ^{125}I-ovine-CRF (^{125}I-o-CRF) (final concentration 150 pM) and 150 µl of the cell homogenate described above. Plates are then allowed to incubate at room temperature for 2 hours before filtering the incubate over GF/F filters (presoaked with 0.3% polyethyleneimine) using an appropriate cell harvester. Filters are rinsed 2 times with ice cold assay buffer before removing individual filters and assessing them for radioactivity on a gamma counter.

Curves of the inhibition of ^{125}I-o-CRF binding to cell membranes at various dilutions of test drug are analyzed by the iterative curve fitting program LIGAND [P.J. Munson and D. Rodbard, *Anal. Biochem.* 107:220 (**1980**)], which provides Ki values for inhibition which are then used to assess biological activity.

A compound is considered to be active if it has a K_i value of less than about 10000 nM for the inhibition of CRF.

Alternatively, tissues and cells which naturally express CRF receptors can be employed in binding assays analogous to those described above.

Inhibition of CRF-Stimulated Adenylate Cyclase Activity

Inhibition of CRF-stimulated adenylate cyclase activity can be performed as described by G. Battaglia et al. *Synapse* **1**:572 (**1987**). Briefly, assays are carried out at 37° C for 10 min in 200 ml of buffer containing 100 mM Tris-HCl (pH 7.4 at 37° C), 10 mM $MgCl_2$, 0.4 mM EGTA, 0.1% BSA, 1 mM isobutylmethylxanthine (IBMX), 250 units/ml phosphocreatine kinase, 5 mM creatine phosphate, 100 mM guanosine 5'-triphosphate, 100 nM oCRF, antagonist peptides (concentration range 10^{-9} to 10^{-6m}) and 0.8 mg original wet weight tissue (approximately 40-60 mg protein). Reactions are initiated by the addition of 1 mM ATP/[^{32}P]ATP (approximately 2-4 mCi/tube) and terminated by the addition of 100 ml of 50 mM Tris-HCL, 45

mM ATP and 2% sodium dodecyl sulfate. In order to monitor the recovery of cAMP, 1 µl of [^{3}H]cAMP (approximately 40,000 dpm) is added to each tube prior to separation. The separation of [^{32}P]cAMP from [^{32}P]ATP is performed by sequential elution over Dowex and alumina columns.

In vivo Biological Assay

The *in vivo* activity of the compounds of the present invention can be assessed using any one of the biological assays available and accepted within the art. Illustrative of these tests include the Acoustic Startle Assay, the Stair Climbing Test, and the Chronic Administration Assay. These and other models useful for the testing of compounds of the present invention have been outlined in C.W. Berridge and A.J. Dunn *Brain Research Reviews* 15:71 (**1990**). Compounds may be tested in any species of rodent or small mammal.

Dosage and Formulation

Compounds of this invention can be administered to treat these abnormalities by means that produce contact of the active agent with the agent's site of action in the body of a mammal. The compounds can be administered by any conventional means available for use in conjunction with pharmaceuticals either as individual therapeutic agent or in combination of therapeutic agents. They can be administered alone, but will generally be administered with a pharmaceutical carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice.

The dosage administered will vary depending on the use and known factors such as pharmacodynamic character of the particular agent, and its mode and route of administration; the recipient's age, weight, and health; nature and extent of symptoms; kind of concurrent treatment; frequency of treatment; and desired effect. For use in the treatment of said diseases or conditions, the compounds of this invention can be orally administered daily at a dosage of the active ingredient of 0.002 to 200 mg/kg of body weight. Ordinarily, a dose of 0.01 to 10 mg/kg in divided doses one to four times

a day, or in sustained release formulation will be effective in obtaining the desired pharmacological effect.

Dosage forms (compositions) suitable for administration contain from about 1 mg to about 100 mg of active ingredient per unit. In these pharmaceutical compositions, the active ingredient will ordinarily be present in an amount of about 0.5 to 95% by weight based on the total weight of the composition.

The active ingredient can be administered orally is solid dosage forms, such as capsules, tablets and powders; or in liquid forms such as elixirs, syrups, and/or suspensions. The compounds of this invention can also be administered parenterally in sterile liquid dose formulations.

Gelatin capsules can be used to contain the active ingredient and a suitable carrier such as but not limited to lactose, starch, magnesium stearate, steric acid, or cellulose derivatives. Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained release products to provide for continuous release of medication over a period of time. Compressed tablets can be sugar-coated or film-coated to mask any unpleasant taste, or used to protect the active ingredients from the atmosphere, or to allow selective disintegration of the tablet in the gastrointestinal tract.

Liquid dose forms for oral administration can contain coloring or flavoring agents to increase patient acceptance.

In general, water, pharmaceutically acceptable oils, saline, aqueous dextrose (glucose), and related sugar solutions and glycols, such as propylene glycol or polyethylene glycol, are suitable carriers for parenteral solutions. Solutions for parenteral administration preferably contain a water soluble salt of the active ingredient, suitable stabilizing agents, and if necessary, butter substances. Antioxidizing agents, such as sodium bisulfite, sodium sulfite, or ascorbic acid, either alone or in combination, are suitable stabilizing agents. Also used are citric acid and its salts, and EDTA. In addition, parenteral

solutions can contain preservatives such as benzalkonium chloride, methyl- or propyl-paraben, and chlorobutanol.

Suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences", A. Osol, a standard reference in the field.

Useful pharmaceutical dosage-forms for administration of the compounds of this invention can be illustrated as follows:

Capsules

A large number of units capsules are prepared by filling standard two-piece hard gelatin capsules each with 100 mg of powdered active ingredient, 150 mg lactose, 50 mg cellulose, and 6 mg magnesium stearate.

Soft Gelatin Capsules

A mixture of active ingredient in a digestible oil such as soybean, cottonseed oil, or olive oil is prepared and injected by means of a positive displacement was pumped into gelatin to form soft gelatin capsules containing 100 mg of the active ingredient. The capsules were washed and dried.

Tablets

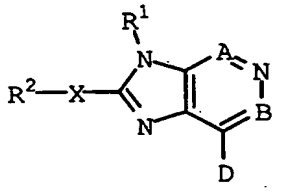
A large number of tablets are prepared by conventional procedures so that the dosage unit was 100 mg active ingredient, 0.2 mg of colloidal silicon dioxide, 5 mg of magnesium stearate, 275 mg of microcrystalline cellulose, 11 mg of starch, and 98.8 mg lactose. Appropriate coatings may be applied to increase palatability or delayed adsorption.

The compounds of this invention may also be used as reagents or standards in the biochemical study of neurological function, dysfunction, and disease.

Obviously, numerous modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims, the invention may be practiced otherwise that as specifically described herein.

WHAT IS CLAIMED AS NEW AND DESIRED TO BE SECURED BY LETTER PATENT OF UNITED STATES IS:

1. A compound of formula (I)



(I)

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

A is N or C-R^7;

B is N or C-R^8;

D is an aryl or heteroaryl group attached through an unsaturated carbon atom;

X is selected from the group CH-R^9, N-R^{10}, O, $S(O)_n$ and a bond;

n is 0, 1 or 2;

R^1 is selected from the group C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-8} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-4} alkoxy-C_{1-4} alkyl, $-SO_2-C_{1-10}$ alkyl, $-SO_2-R^{1a}$, and $-SO_2-R^{1b}$;

R^1 is substituted with 0-1 substituents selected from the group -CN, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-CO_2R^{13a}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-CONR^{13a}R^{16a}$, 1-morpholinyl, 1-piperidinyl, 1-piperazinyl, and C_{3-8} cycloalkyl, wherein 0-1 carbon atoms in the C_{4-8} cycloalkyl is replaced by a group selected from the group -O-, $-S(O)_n-$, $-NR^{13a}-$, $-NCO_2R^{14b}-$, $-NCOR^{14b}-$ and

$-NSO_2R^{14b}-$, and wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^1 is also substituted with 0-3 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, R^{1c}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, I, C_{1-4} haloalkyl, $-OR^{13a}$, $-NR^{13a}R^{16a}$, C_{1-4} alkoxy-C_{1-4} alkyl, and C_{3-8} cycloalkyl which is substituted with 0-1 R^9 and in which 0-1 carbons of C_{4-8} cycloalkyl is replaced by -O-;

provided that R^1 is other than a cyclohexyl-$(CH_2)_2$- group;

R^{1a} is aryl and is selected from the group phenyl, naphthyl, indanyl and indenyl, each R^{1a} being substituted with 0-1 $-OR^{17}$ and 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$;

R^{1b} is heteroaryl and is selected from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-onyl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$,

$-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^{1c} is heterocyclyl and is a saturated or partially saturated heteroaryl, each heterocyclyl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{13a}$, SH, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-OC(O)R^{14b}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-NR^{13a}R^{16a}$, and $-CONR^{13a}R^{16a}$ and each heterocyclyl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b} and wherein any sulfur atom is optionally monooxidized or dioxidized;

provided that R^1 is other than a $-(CH_2)_{1-4}$-aryl, $-(CH_2)_{1-4}$-heteroaryl, or $-(CH_2)_{1-4}$-heterocycle, wherein the aryl, heteroaryl, or heterocycle group is substituted or unsubstituted;

R^2 is selected from the group C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{2-4} alkenyl, and C_{2-4} alkynyl and is substituted with 0-3 substituents selected from the group -CN, hydroxy, halo and C_{1-4} alkoxy;

alternatively R^2, in the case where X is a bond, is selected from the group -CN, CF_3 and C_2F_5;

R^7 and R^8 are independently selected at each occurrence from the group H, Br, Cl, F, I, -CN, C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, $(C_{1-4}$ alkyl$)_2$amino and phenyl, each phenyl is substituted with 0-3 groups selected from the group C_{1-7} alkyl, C_{3-8} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkyl

sulfinyl, C_{1-4} alkylsulfonyl, C_{1-6} alkylamino and (C_{1-4} alkyl)$_2$amino;

R^9 and R^{10} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-6} cycloalkyl-C_{1-4} alkyl and C_{3-8} cycloalkyl;

R^{13} is selected from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, aryl, aryl(C_{1-4} alkyl)-, heteroaryl and heteroaryl(C_{1-4} alkyl)-;

R^{13a} and R^{16a} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{14} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, aryl, aryl(C_{1-4} alkyl)-, heteroaryl and heteroaryl(C_{1-4} alkyl)- and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy C_{1-4} haloalkoxy, and dimethylamino;

R^{14a} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{14b} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{15} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, phenyl and benzyl, each phenyl or benzyl being substituted on the aryl moiety with 0-3 groups chosen from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{15a} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{17} is selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{1-4} haloalkyl, $R^{14}S(O)_n$-C_{1-4} alkyl, and $R^{17b}R^{19b}N$-C_{2-4} alkyl;

R^{18} and R^{19} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{1-4} haloalkyl;

alternatively, in an $NR^{17}R^{19}$ moiety, R^{17} and R^{19} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

alternatively, in an $NR^{17b}R^{19b}$ moiety, R^{17b} and R^{19b} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

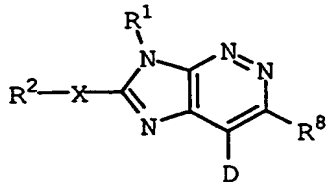
R^{17a} and R^{19a} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and C_{1-4} haloalkyl;

aryl is independently selected at each occurrence from the group phenyl, naphthyl, indanyl and indenyl, each aryl being substituted with 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, methylenedioxy, C_{1-4} alkoxy-C_{1-4} alkoxy, $-OR^{17}$, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, $-NO_2$, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and up to 1 phenyl, each phenyl substituent being substituted with 0-4 substituents selected from the group C_{1-3} alkyl, C_{1-3} alkoxy, Br, Cl, F, I, -CN, dimethylamino, CF_3, C_2F_5, OCF_3, SO_2Me and acetyl;

heteroaryl is independently selected at each occurence from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-on-yl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15}, CO_2R^{14a}, COR^{14a} and SO_2R^{14a}; and,

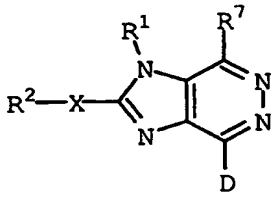
provided that when D is imidazole or triazole, R^1 is other than unsubstituted C_{1-6} linear or branched alkyl or C_{3-6} cycloalkyl.

2. A compound according to Claim 1, wherein the compound is of formula Ia:



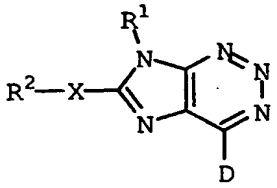
(Ia).

3. A compound according to Claim 1, wherein the compound is of formula Ib:



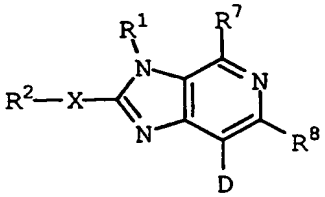
(Ib).

4. A compound according to Claim 1, wherein the compound is of formula Ic:



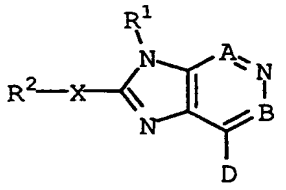
(Ic).

5. A compound according to Claim 1, wherein the compound is of formula Id:



(Id).

6. A method of treating affective disorder, anxiety, depression, headache, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, epilepsy, stroke, ulcers, amyotrophic lateral sclerosis, hypoglycemia or a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, in mammals, comprising: administering to the mammal a therapeutically effective amount of a compound of formula (I):



(I)

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

A is N or C-R^7;

B is N or C-R^8;

D is an aryl or heteroaryl group attached through an unsaturated carbon atom;

X is selected from the group CH-R^9, N-R^{10}, O, $S(O)_n$ and a bond;

n is 0, 1 or 2;

R^1 is selected from the group C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-8} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-4} alkoxy-C_{1-4} alkyl, $-SO_2-C_{1-10}$ alkyl, $-SO_2-R^{1a}$, and $-SO_2-R^{1b}$;

R^1 is substituted with 0-1 substituents selected from the group -CN, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-CO_2R^{13a}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-CONR^{13a}R^{16a}$, 1-morpholinyl, 1-piperidinyl, 1-piperazinyl, and C_{3-8} cycloalkyl, wherein 0-1 carbon atoms in the C_{4-8} cycloalkyl is replaced by a group selected from the group -O-, $-S(O)_n-$, $-NR^{13a}-$, $-NCO_2R^{14b}-$, $-NCOR^{14b}-$ and $-NSO_2R^{14b}-$, and wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^1 is also substituted with 0-3 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, R^{1c}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, I, C_{1-4} haloalkyl, $-OR^{13a}$, $-NR^{13a}R^{16a}$, C_{1-4} alkoxy-C_{1-4} alkyl, and C_{3-8} cycloalkyl which is substituted with 0-1 R^9 and in which 0-1 carbons of C_{4-8} cycloalkyl is replaced by -O-;

R^{1a} is aryl and is selected from the group phenyl, naphthyl, indanyl and indenyl, each R^{1a} being substituted with 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$;

R^{1b} is heteroaryl and is selected from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, pyrazolyl,

triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-onyl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^{1c} is heterocyclyl and is a saturated or partially saturated heteroaryl, each heterocyclyl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{13a}$, SH, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-OC(O)R^{14b}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-NR^{13a}R^{16a}$, and $-CONR^{13a}R^{16a}$ and each heterocyclyl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b} and wherein any sulfur atom is optionally monooxidized or dioxidized;

R^2 is selected from the group C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{2-4} alkenyl, and C_{2-4} alkynyl and is substituted with 0-3 substituents selected from the group -CN, hydroxy, halo and C_{1-4} alkoxy;

alternatively R^2, in the case where X is a bond, is selected from the group -CN, CF_3 and C_2F_5;

R^7 and R^8 are independently selected at each occurrence from the group H, Br, Cl, F, I, -CN, C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4}

alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, $(C_{1-4}$ alkyl$)_2$amino and phenyl, each phenyl is substituted with 0-3 groups selected from the group C_{1-7} alkyl, C_{3-8} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkyl sulfinyl, C_{1-4} alkylsulfonyl, C_{1-6} alkylamino and $(C_{1-4}$ alkyl$)_2$amino;

R^9 and R^{10} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-6} cycloalkyl-C_{1-4} alkyl and C_{3-8} cycloalkyl;

R^{13} is selected from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, aryl, aryl$(C_{1-4}$ alkyl$)$-, heteroaryl and heteroaryl$(C_{1-4}$ alkyl$)$-;

R^{13a} and R^{16a} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{14} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, aryl, aryl$(C_{1-4}$ alkyl$)$-, heteroaryl and heteroaryl$(C_{1-4}$ alkyl$)$- and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy C_{1-4} haloalkoxy, and dimethylamino;

R^{14a} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{14b} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{15} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, phenyl and benzyl, each phenyl or benzyl being substituted on the aryl moiety with 0-3 groups chosen from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{15a} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{17} is selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{1-4} haloalkyl, $R^{14}S(O)_n$-C_{1-4} alkyl, and $R^{17b}R^{19b}N$-C_{2-4} alkyl;

R^{18} and R^{19} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{1-4} haloalkyl;

alternatively, in an $NR^{17}R^{19}$ moiety, R^{17} and R^{19} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

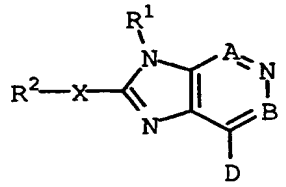
alternatively, in an $NR^{17b}R^{19b}$ moiety, R^{17b} and R^{19b} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

R^{17a} and R^{19a} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and C_{1-4} haloalkyl;

aryl is independently selected at each occurrence from the group phenyl, naphthyl, indanyl and indenyl, each aryl being substituted with 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, methylenedioxy, C_{1-4} alkoxy-C_{1-4} alkoxy, $-OR^{17}$, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, $-NO_2$, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and up to 1 phenyl, each phenyl substituent being substituted with 0-4 substituents selected from the group C_{1-3} alkyl, C_{1-3} alkoxy, Br, Cl, F, I, -CN, dimethylamino, CF_3, C_2F_5, OCF_3, SO_2Me and acetyl; and,

heteroaryl is independently selected at each occurence from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-on-yl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15}, CO_2R^{14a}, COR^{14a} and SO_2R^{14a}.

7. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula (I):



(I)

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

A is N or C-R^7;

B is N or C-R^8;

D is an aryl or heteroaryl group attached through an unsaturated carbon atom;

X is selected from the group CH-R^9, N-R^{10}, O, $S(O)_n$ and a bond;

n is 0, 1 or 2;

R^1 is selected from the group C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-8} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-4} alkoxy-C_{1-4} alkyl, $-SO_2-C_{1-10}$ alkyl, $-SO_2-R^{1a}$, and $-SO_2-R^{1b}$;

R^1 is substituted with 0-1 substituents selected from the group -CN, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-CO_2R^{13a}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-CONR^{13a}R^{16a}$, 1-morpholinyl, 1-piperidinyl, 1-piperazinyl, and C_{3-8} cycloalkyl, wherein 0-1 carbon atoms in the C_{4-8} cycloalkyl is replaced by a group selected from the group -O-, $-S(O)_n-$, $-NR^{13a}-$, $-NCO_2R^{14b}-$, $-NCOR^{14b}-$ and $-NSO_2R^{14b}-$, and wherein N_4 in 1-piperazinyl is

substituted with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^1 is also substituted with 0-3 substituents independently selected at each occurrence from the group R^{1a}, R^{1b}, R^{1c}, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, Br, Cl, F, I, C_{1-4} haloalkyl, $-OR^{13a}$, $-NR^{13a}R^{16a}$, C_{1-4} alkoxy-C_{1-4} alkyl, and C_{3-8} cycloalkyl which is substituted with 0-1 R^9 and in which 0-1 carbons of C_{4-8} cycloalkyl is replaced by -O-;

R^{1a} is aryl and is selected from the group phenyl, naphthyl, indanyl and indenyl, each R^{1a} being substituted with 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$;

R^{1b} is heteroaryl and is selected from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-onyl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-OC(O)R^{18}$, $-NR^{15a}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15a}CONR^{17a}R^{19a}$, $-NR^{15a}CO_2R^{18}$, $-NR^{17a}R^{19a}$, and $-CONR^{17a}R^{19a}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b};

R^{1c} is heterocyclyl and is a saturated or partially saturated heteroaryl, each heterocyclyl being substituted on 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{13a}$, SH, $-S(O)_nR^{14b}$, $-COR^{13a}$, $-OC(O)R^{14b}$, $-NR^{15a}COR^{13a}$, $-N(COR^{13a})_2$, $-NR^{15a}CONR^{13a}R^{16a}$, $-NR^{15a}CO_2R^{14b}$, $-NR^{13a}R^{16a}$, and $-CONR^{13a}R^{16a}$ and each heterocyclyl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{13a}, CO_2R^{14b}, COR^{14b} and SO_2R^{14b} and wherein any sulfur atom is optionally monooxidized or dioxidized;

R^2 is selected from the group C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{2-4} alkenyl, and C_{2-4} alkynyl and is substituted with 0-3 substituents selected from the group -CN, hydroxy, halo and C_{1-4} alkoxy;

alternatively R^2, in the case where X is a bond, is selected from the group -CN, CF_3 and C_2F_5;

R^7 and R^8 are independently selected at each occurrence from the group H, Br, Cl, F, I, -CN, C_{1-4} alkyl, C_{3-8} cycloalkyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, $(C_{1-4}$ alkyl$)_2$amino and phenyl, each phenyl is substituted with 0-3 groups selected from the group C_{1-7} alkyl, C_{3-8} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkyl sulfinyl, C_{1-4} alkylsulfonyl, C_{1-6} alkylamino and $(C_{1-4}$ alkyl$)_2$amino;

R^9 and R^{10} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-6} cycloalkyl-C_{1-4} alkyl and C_{3-8} cycloalkyl;

R^{13} is selected from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-

C_{1-6} alkyl, aryl, aryl(C_{1-4} alkyl)-, heteroaryl and heteroaryl(C_{1-4} alkyl)-;

R^{13a} and R^{16a} are independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{14} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, aryl, aryl(C_{1-4} alkyl)-, heteroaryl and heteroaryl(C_{1-4} alkyl)- and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy C_{1-4} haloalkoxy, and dimethylamino;

R^{14a} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{14b} is selected from the group C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy-C_{1-4} alkyl, C_{3-6} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{15} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, phenyl and benzyl, each phenyl or benzyl being substituted on the aryl moiety with 0-3 groups chosen from the group C_{1-4} alkyl, Br, Cl, F, I, C_{1-4} haloalkyl, nitro, C_{1-4} alkoxy, C_{1-4} haloalkoxy, and dimethylamino;

R^{15a} is independently selected at each occurrence from the group H, C_{1-4} alkyl, C_{3-7} cycloalkyl, and C_{3-6} cycloalkyl-C_{1-6} alkyl;

R^{17} is selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, C_{1-4} haloalkyl, $R^{14}S(O)_n$-C_{1-4} alkyl, and $R^{17b}R^{19b}N$-C_{2-4} alkyl;

R^{18} and R^{19} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl, C_{1-2} alkoxy-C_{1-2} alkyl, and C_{1-4} haloalkyl;

alternatively, in an $NR^{17}R^{19}$ moiety, R^{17} and R^{19} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

alternatively, in an $NR^{17b}R^{19b}$ moiety, R^{17b} and R^{19b} taken together form 1-pyrrolidinyl, 1-morpholinyl, 1-piperidinyl or 1-piperazinyl, wherein N_4 in 1-piperazinyl is substituted with 0-1 substituents selected from the group R^{13}, CO_2R^{14}, COR^{14} and SO_2R^{14};

R^{17a} and R^{19a} are independently selected at each occurrence from the group H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl and C_{1-4} haloalkyl;

aryl is independently selected at each occurrence from the group phenyl, naphthyl, indanyl and indenyl, each aryl being substituted with 0-5 substituents independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, methylenedioxy, C_{1-4} alkoxy-C_{1-4} alkoxy, $-OR^{17}$, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, $-NO_2$, SH, $-S(O)_nR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and up to 1 phenyl, each phenyl substituent being substituted with 0-4 substituents selected from the

group C_{1-3} alkyl, C_{1-3} alkoxy, Br, Cl, F, I, -CN, dimethylamino, CF_3, C_2F_5, OCF_3, SO_2Me and acetyl; and,

heteroaryl is independently selected at each occurence from the group pyridyl, pyrimidinyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, indolinyl, benzoxazolin-2-on-yl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C_{1-6} alkyl, C_{3-6} cycloalkyl, Br, Cl, F, I, C_{1-4} haloalkyl, -CN, nitro, $-OR^{17}$, SH, $-S(O)_mR^{18}$, $-COR^{17}$, $-CO_2R^{17}$, $-OC(O)R^{18}$, $-NR^{15}COR^{17}$, $-N(COR^{17})_2$, $-NR^{15}CONR^{17}R^{19}$, $-NR^{15}CO_2R^{18}$, $-NR^{17}R^{19}$, and $-CONR^{17}R^{19}$ and each heteroaryl being substituted on any nitrogen atom with 0-1 substituents selected from the group R^{15}, CO_2R^{14a}, COR^{14a} and SO_2R^{14a}.

INTERNATIONAL SEARCH REPORT

Inter ɔnal Application No
PCT/US 99/14935

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D487/04 A61K31/5025 C07D471/04 A61K31/5365 A61K31/437
//(C07D487/04,237:00,235:00),(C07D471/04,235:00,221:00),
(C07D487/04,253:00,235:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 812 831 A (PFIZER) 17 December 1997 (1997-12-17) claims 1,8	1,7
P,X	WO 98 35967 A (NEUROCRINE BIOSCIENCES) 20 August 1998 (1998-08-20) claims 4,5	1,7

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 November 1999	19/11/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Alfaro Faus, I

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INTERNATIONAL SEARCH REPORT

...ormation on patent family members

Inter: ...nal Application No
PCT/US 99/14935

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EP 812831 A	17-12-1997	CA 2207348 A	11-12-1997
		JP 10072449 A	17-03-1998
WO 9835967 A	20-08-1998	AU 6279598 A	08-09-1998